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(54) Title: COLLECTION OF PROKARYOTIC DNA FOR TWO HYBRID SYSTEMS HELICOBACTER PYLORI PROTEIN-PROTEIN INTERACTIONS AND APPLICATION THEREOF

(57) Abstract: The present invention concerns collections of recombinant cell clones derived from a prokaryotic genome, more particularly from Helicobacter pylori genome, usable for two-hybrid systems and methods to produce such collections. The invention further relates to the identification of H. pylori protein-protein interactions and to the application of said collections of recombinant cell clones and said identified proteins interactions to the pharmaceutical and diagnostic field.

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AMENDED CLAIMS

[received by the International Bureau on 28 November 2000 (28.11.00); original claim 60 amended; remaining claims unchanged (2 pages)]

- b) a polynucleotide having the sequence identified by the reference indicated in the right column "SID®" in table III;
- c) fragment having at least 12 consecutive nucleotides of polynucleotide of a) or b), complement thereof, and RNA corresponding to said polynucleotide; and
- d) a polynucleotide having at least 80 % identity degree after alignment to a nucleic acid sequence of a polynucleotide of a) or b);

with the exception of the polynucleotides encoding the polypeptide having the sequence disclosed in the EMBL Data base document Accession number 025045.

- 61. Purified or isolated polypeptide selected from the group consisting of:
- a) a polypeptide having an amino acids sequence identified by the reference indicated in the right column "SID®" in table II, and fragment thereof having at least 5 consecutive amino acids; and
 - b) a polypeptide encoded by a polynucleotide according to claim 59 or 60.
- 62. Use of a polynucleotide according to claim 60 as a primer for amplification.
 - 63. Use of a polynucleotide according to claim 60 as a specific probe for detection.
 - 64. Cloning or expression vector containing a polynucleotide according to anyone of claims 59 and 60.
- 65. Vector according to claim 64, wherein the vector is the plasmid pACTIIst, pAS2ΔΔ or pP6.
- 66. Vector according to claim 64, wherein the vector is the plasmid selected from the group consisting of pT25, pKT25, pUT18 and pUT18C.
 - 67. Vector according to claim 64, wherein the vector is self replicated.
 - 68. Vector according to claim 64 or 67, wherein the vector is a viral vector.
- 69. Vector according to claim 68, wherein the vector is chosen between an adenovirus, AAV, a retrovirus, a proxivirus or an herpes virus.
- 70. Vector according to anyone of claims 64 to 69 including elements allowing expression and/or secretion of said polynucleotide in a host cell.
- Host cell transformed with a vector according to anyone of claims 64 to 70.

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Host cell according to claim 71, wherein the host cell is a prokaryotic **72**. cell.

Host cell according to claim 71, wherein the host cell is an eukaryotic **73**. cell.

Method for producing a polypeptide according to anyone of claims 45 *7*4. and 61, comprising the steps of:

a) cultivating a host cell according to anyone of claims 71 to 73 under conditions and in culture medium allowing the growth of said host cell and the expression of said polypeptide; and

b) recovering said polypeptide directly from the culture medium or from said cultivated cell obtained in step a).

Purified or isolated polypeptide obtained by the method according to 75. claim 74.

A method for selecting an agent capable of modulating the protein-76. protein interaction of a step of two polypeptides according to claim 45 comprising the steps of:

a) cultivating a recombinant cell clone containing a reporter gene expression of which is toxic for said recombinant cell clone and transformed with two plasmids wherein:

i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and a DNA binding domain;

ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and an activating domain capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting;

on a selective medium containing the agent to be tested and allowing the growth of said recombinant cell clone when the toxic reporter gene is not activated; and

b) selecting agent which is capable of inhibiting the growth of the recombinant cell clone cultivated in step a).

A method for selecting an agent capable of modulating the proteinprotein interaction of a set of two polypeptides according to claim 45 comprising the steps of:

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specific site on the DNA and a domain that is necessary for activation (Keegan et al., 1986, Science, 231(4739): 699-704 Separation of DNA binding from the transcription activating function of eukaryotic regulatory protein).

To date however, the two-hybrid assay system has not been specifically applied to the systematic study of prokaryotic protein-protein interactions although number of diseases are due to prokaryotic microorganisms.

One of the prokaryotic microorganisms presenting a great interest is *Helicobacter* pylori. Helicobacter pylori (H. pylori) is a microaerophilic, Gram negative, slow growing, spiral shaped and flagellated organism. H. pylori has been first isolated in 1983 from gastric biopsy specimen of patient with chronic gastritis (Marshall et al., 1984, Lancet, i:1311-1314, Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration).

Helicobacter pylori has become identified as a primary cause of chronic gastroduodenal disorders, such as gastritis, dyspepsia, and peptic ulcers, in humans. Studies have shown (Labigne et al.) that *H. pylori* can be successfully eradicated by a treatment combining two antibiotics with a proton pump inhibitor. However, few antibiotics are active against *H. pylori*, and antibiotic-resistant strains have begun to appear.

H. pylori strain n° 26695 genome has been studied by Tomb et al. (Tomb et al., 1997, Nature, vol. 388, 539-547, The complete genome sequence of the gastric pathogen Helicobacter pylori). This strain's genome consists of a circular chromosome with a size of 1,667,867 bp, average G + C content of 39 %, and 1590 predicted coding sequences (open reading frames or "ORF").

The bacterial factors necessary for colonization of the gastric environment, and for virulence of this pathogen, are poorly understood. Examples of known virulence factors are:

- Enzymes involved in neutralizing the acid gastric pH: the multisubunit urease is a characteristic enzyme that is crucial for survival in acidic pH and for successful colonization of the gastric environment, a site that few other microbes can colonize (Labigne et al., WO 93/07273, *Helicobacter pylori* genes necessary for the regulation and maturation of urease, and use thereof). Genes encoding ureases have been located

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on a 34 kb chromosome fragment and comprise ureA, ureB, ureC, ureD, ureE, ureF, ureG, ureH and ureI.

- Bacterial flagellar proteins responsible for motility across the mucous layer (Hazell et al., 1986, J. Inf. Dis., 153, 658-663 Campylobacter pyloridis and gatritis: association with intracellular spaces and adaptation to an environment of mucus as important factors in colonization of the gastric epithelium; Leying et al., 1992, Mol. Microbiol., 6, 2863-2874 Cloning and genetic characterization of Helicobacter pylori flagellin gene): flagellar filaments biosynthesis comprises A and B flagellins and the filament cap. These two biosyntheses are regulated by flbA gene (Suerbaum et al., French patent application, 1995, N 2 736 360, Cloning and characterization of flbA gene of Helicobacter pylori, aflagellated strains production).

- Two other essential toxins for virulence are VacA and CagA:

- VacA is a *H. pylori* toxin that induces the formation of large acidic vacuoles in host epithelial cells. These large vacuoles originate from massive swelling of membranous compartments of late stages of the endocytic pathway (de Bernard et al., 1997, Microbiology, 26(4), 665-674, *Helicobacter pylori* toxin VacA induces vacuole formation by acting in the cell cytosol). Proof for receptor-mediated interaction with VacA has been made by Pagliaccia et al.; m2 allele of vacA gene has always been described as inactive in the in vitro HeLa cell assay, however, the m2 allele is associated with peptic ulcer and is prevalent in populations in which peptic ulcer and gastric cancer have high incidence (Pagliaccia et al., Proc. Natl. Acad. Sci. U.S.A, 1998, 95(17), 10212-10217, The m2 form of the *Helicobacter pylori* cytotoxin has cell type-specific vacuolating activity).

- CagA is one of the proteins encoded by the "cag pathogenicity island" (Spohn et al. 1997, Molecular Microbiology, 26(2), 361-372, Transcriptional analysis of the divergent cagAB genes encoded by the pathogenicity island of *Helicobacter pylori*) found in *H. pylori* strains isolated from most patients with peptic ulcer disease and adenocarcinoma. CagA is produced by 50-60 % of *H. pylori* strains; it is a high molecular weight (120-140 kDa) superficial protein and an immunodominant antigen with unknown function. *H. pylori* strains that produce CagA protein have two genes cagB and cagC (36 and 101 kDa proteins, respectively). These genes are highly

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associated with duodenal ulcers (Blaser et al. 1996, WO 96/12825, cagB and cagC genes of *Helicobacter pylori* and related methods and compositions).

- Other virulence factors are : several gastric tissue-specific adhesins (Boren et al., 1993, Science, 262, 1892-1895).

Therapeutic agents are currently available that eradicate *H. pylori* infections *in vitro*. However, methods employing antibiotic agents result in the emergence of bacterial strains which are resistant to these agents.

As number of diseases are due to prokaryotic microorganisms, there is a great need for new tools directed to the functional and global study of these newly characterized complete or partial genome, particurlarly *Escherichia coli* genome, but also of pathogenic microorganisms such as *H. pylori*, *Staphylococcus aureus* and *Streptococcus pneumoniae* genomes.

In addition to the need for these new tools, there is also and especially a need to find new E. coli, H. pylori, S. aureus and S. pneumoniae protein-protein interactions for the development of more effective and better targeted therapeutic.

Summary of the invention

The present invention relates to a method for producing a collection of recombinant cell clones usable for two-hybrid systems containing genomic DNA fragments of prokaryotic micro-organism, particularly of *E. coli*, *H. pylori*, *S. aureus* and *S. pneumoniae*, to collection of recombinant cell clones obtainable by this method and kit for screening comprising said collection.

The invention is also directed to a yeast or bacterial two-hybrid system method for identifying a recombinant cell clone expressing a prey polypeptide of a prokaryotic microorganism capable of interacting with a bait polypeptide and a method for identifying said prey polypeptide.

The present invention further comprises polynucleotides or polypeptides corresponding to the prey polypeptides capable of interacting with a bait polypeptide and the protein-protein interactions identified by the yeast or bacterial two-hybrid system method according to the invention, vectors and host cells containing said polynucleotides, and pharmaceutical composition including them.

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The present invention also concerns a method for identifying a polynucleotide encoding a selected interacting domain (SID®) of a prey polypeptide of interest from a prokaryotic microorganism capable of interacting with a bait polypeptide.

Another aspect of the present invention relates to a method for selecting an agent capable of modulating the protein-protein interaction identified by the yeast or bacterial two-hybrid system method according to the invention.

Brief description of the drawings

Figure 1 is a restriction map of the plasmid pAS2ΔΔ which may be used for the veast two-hybrid system.

Figure 2 is a restriction map of the plasmid pACTIIst which may be used for the yeast two-hybrid system.

Figure 3 is a restriction map of the plasmid pUT18 which may be used for the bacterial two-hybrid system. In this figure, each multicloning site (MCS) is detailled.

Figure 4 is a restriction map of the plasmid pUT18C which may be used for the bacterial two-hybrid system. In this figure, each multicloning site (MCS) is detailled.

Figure 5 is a restriction map of the plasmid pT25 which may be used for the bacterial two-hybrid system. In this figure, each multicloning site (MCS) is detailled.

Figure 6 is a restriction map of the plasmid pKT25 which may be used for the bacterial two-hybrid system. In this figure, each multicloning site (MCS) is detailled.

Figure 7 is a schematic representation of the SID® identification method. In this figure, the « Full-length prey protein » is the Open Reading Frame where the identified prey polypeptides are included, the Selected Interaction Domain SID® is determined by comparison of every prey polypeptide fragment.

Figure 8 is a restriction map of the plasmid pP6 which may be used for the yeast two-hybrid system.

Detailed description of the invention

The present invention is directed to a method for producing a collection of recombinant cell clones usable for two-hybrid systems comprising the steps of:

a) fragmenting DNA;

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- b) inserting polynucleotidic fragments obtained in step a) in plasmids in such a way that the expression of said plasmids in host cell leads to an hybrid polypeptide containing a specific domain capable of activating a reporter gene when associated with a complementary domain;
- 5 c) transforming cell clones with plasmids obtained in step b); and
 - d) optionally, selecting the transformed recombinant cell clones obtained in step c); wherein DNA of step a) is genomic DNA obtained from a prokaryotic micro-organism.

The step a) of fragmenting DNA according to the method of the invention may be obtained by enzyme digestion, sonication or nebulization of the source of genomic DNA, sonication and nebulization ensuring a random cleavage of the starting DNA material and thus an excellent representation of all the possible inserts.

In a preferred embodiment, the step a) of fragmenting DNA of the method according to the invention is carried out by a nebulization process, for example, with a commercial nebulizer (GATC).

In a preferred embodiment, the plasmid used in the method for producing a collection of recombinant cell clones usable for two-hybrid systems according to the present invention may comprise in addition a nucleic sequence encoding a promoter, a multicloning site, a terminator site and a selection marker, operably linked.

A "promoter" refers to a DNA sequence recognized by the transcriptional machinery of the cell required to initiate the specific transcription of a gene.

A sequence which is "operably linked" to a regulatory sequence such as a promoter means that said regulatory element is in the correct location and orientation in relation to the nucleic acid to control RNA polymerase initiation and expression of the nucleic acid of interest. As used herein, the term "operably linked" refers to a linkage of polynucleotide elements in a functional relationship. For instance, a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the coding sequence. More precisely, two DNA molecules (such as a polynucleotide containing a promoter region and a polynucleotide encoding a desired polypeptide or polynucleotide) are said to be "operably linked" if the nature of the linkage between the two polynucleotides does not (1) result in the introduction of a frame-shift mutation or (2) interfere with the ability of the polynucleotide containing the promoter to direct the transcription of the coding polynucleotide.

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As a promoter, one could use full or truncated ADH promoter.

By specific domain, it is intended a domain whose association with a complementary domain leads to the activation of a reporter gene.

In one particular embodiment of this invention, the specific domain may be a transcriptional activating domain or a DNA-binding domain and the complementary domain may, respectively, be a DNA binding domain or a transcriptional activation domain.

Transcriptional activating domain and DNA-binding domain may be derived from Gal4 and LexA respectively.

In another particular embodiment of the invention, the activation domain is a part of an enzyme and the complementary domain is the other part of the same enzyme. Proximity of the two parts of the enzyme may restore the enzyme activity and activate a reporter gene.

For example, specific and complementary domain may be T25 and T18 polypeptides that constitute the catalytic domain of *Bordetella pertussis* adenylate cyclase.

The reporter gene may be contained either in a plasmid of recombinant cell clone or in its genome.

As an illustrative embodiment of the invention, the reporter gene is chosen among the group consisting in a nutritional gene or also a gene the expression of which is visualized by colorimetry such as His3, LacZ or both LacZ and His3.

As a selective marker, gene encoding for a toxin, color marker of the type of the Green Fluorescent Protein (GFP), gene encoding for phage receptor proteins or fragment thereof such as phage λ receptor lam B and any other gene giving selectable phenotype, resistance gene, such as ampicilline, kanamycin, tetracyclin or lactose or maltose nutritional gene, may be used.

In a particularly preferred embodiment, the invention relates to a method according to the invention wherein DNA of step a) is genomic DNA obtained from *Helicobacter pylori* (see example 1.A.), *Escherichia coli*, *Staphylococcus aureus* and *Streptococcus pneumoniae*.

The invention also concerns a collection of recombinant cell clones usable for two-hybrid systems obtainable by a method according to the invention.

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The invention further concerns a collection of recombinant cell clones usable for two-hybrid systems, each recombinant cell clone containing a polynucleotide inserted in a plasmid whose expression leads to hybrid polypeptide containing a specific domain, wherein the said polynucleotide is a genomic DNA fragment obtained from a prokaryotic micro-organism.

In a preferred embodiment, said genomic DNA fragment is obtained by a fragmentation process by nebulization.

In a particularly preferred embodiment, the invention relates to collection of recombinant cell clones of the invention wherein the prokaryotic micro-organism is Helicobacter pylori, Escherichia coli, Staphylococcus aureus and Streptococcus pneumoniae.

The present invention also comprises a collection of recombinant cell clones according to the invention, wherein the recombinant cell clones are selected from the group consisting of Gram+ or Gram- bacteria, yeasts, fungi and mammalian cells, particularly from the group consisting of *Escherichia coli* bacteria and *Saccharomyces cerevisiae* yeast.

The present invention further concerns a collection of recombinant cell clones according to the invention, wherein the plasmids comprise at least a nucleic sequence coding a promoter, a specific domain, a multicloning site where the said polypeptide is cloned, and a selection marker.

In a preferred embodiment, the present invention further concerns a collection of recombinant cell clones according to the invention, wherein the polynucleotide is inserted in the plasmid pACTIIst or in the plasmid pP6.

In a more preferred embodiment, the present invention further concerns a collection of recombinant cell clones according to the invention, wherein the collection contains 10^6 to 10^7 or to 10^8 recombinant *Escherichia coli* clones and wherein the proportion of independent cell clones with insert is at least 60 %, 70 %, 80 %, 90 %, 95 % or 97 %.

The present invention particularly comprises the collection of recombinant cell clones according to the invention which has been deposited in the Collection National de Cultures de Microorganismes (CNCM) (France, Paris) on April 13, 1999 under the

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accession number I-2181, and on March 23, 2000 under the accession numbers I-2416, I-2414, I-2415 and I-2417.

The collection of recombinant cell clones which has been deposited under the accession number I-2181 (identification reference: HGXBHP1) concerns a genomic librairy of *Helicobacter pylori* 26695 strain, cloned in the stop bis pACTII vector, transformed in *Escherichia coli* DH10B. The collection contains about 10⁷ independent clones with an insert pourcentage of about 97 % and an insert average size of 1000 pb.

The collection of recombinant cell clones which has been deposited under the accession number I-2416 (identification reference: HGXBSA1) concerns a genomic librairy of *Staphylococcus aureus* col strain, cloned in the pP6 vector, transformed in *Escherichia coli* DH10B. The collection contains about 6.8 10⁷ independent clones with an insert pourcentage superior to 95 % and an insert average size of 1100 pb.

The collection of recombinant cell clones which has been deposited under the accession number I-2415 (identification reference: HGXBEC1) concerns a genomic librairy of *Escherichia coli* MG1655 strain, cloned in the pP6 vector, transformed in *Escherichia coli* DH10B. The collection contains about 3 10⁷ independent clones with an insert pourcentage superior to 98 % and an insert average size of 853 pb.

The collection of recombinant cell clones which has been deposited under the accession number I-2417 (identification reference: HGXBHP4) concerns a genomic librairy of *Helicobacter pylori* 26695 strain, cloned in the pP6 vector, transformed in *Escherichia coli* DH10B. The collection contains about 1.9 10⁷ independent clones with an insert pourcentage superior to 98 % and an insert average size of 1009 pb.

In another aspect, the present invention relates to a collection of recombinant cell clones according to the invention, wherein the collection contains 10^5 to 1.5×10^7 haploid recombinant *Saccharomyces cerevisiae* clones and wherein the proportion of independant cell clones with insert is at least 60 %, 70 %, 80 %, 90 %, 95 % or 97 %.

The present invention particularly comprises the collection of recombinant cell clones according to the invention which has been deposited in the Collection National de Cultures de Microorganismes (CNCM) on April 13, 1999 under the accession

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number I-2182, and on March 23, 2000 under the accession numbers I-2420, I-2419 and I-2418.

The collection of recombinant cell clones which has been deposited under the accession number I-2182 (identification reference: HGXYHP1) concerns a genomic librairy of *Helicobacter pylori*, 26195 strain, which has been amplified in *E. coli* (HGXBHP1 librairy), cloned in the stop bis pACTII vector, transformed in *Saccharomyces cerevisiae*, Y187 strain, and containing about 2 10⁶ independent clones.

The collection of recombinant cell clones which has been deposited under the accession number I-2420 (identification reference: Lib Sa2) concerns a genomic librairy of *Staphylococcus aureus*, col strain, which has been amplified in *E. coli* (HGXBSA1 librairy), cloned in the pP6 vector, transformed in *Saccharomyces cerevisiae*, Y187 strain, containing about 2.2 10⁶ independent clones, and a cell concentration about 5 10⁸ cells/ml.

The collection of recombinant cell clones which has been deposited under the accession number I-2419 (identification reference: Sp in Y187 pP6) concerns a genomic librairy of *Streptococcus pneumoniae*, type 4 strain, which has been amplified in *E. coli* (HGXBSP1 librairy), cloned in the pP6 vector, transformed in *Saccharomyces cerevisiae*, Y187 strain, containing about 2.8 10⁶ independent clones, and a cell concentration about 5 10⁸ cells/ml.

The collection of recombinant cell clones which has been deposited under the accession number I-2418 (identification reference: E.coli in Y187 lib1) concerns a genomic librairy of *Escherichia coli*, MG1655 strain, which has been amplified in *E. coli* (HGXBEC1 librairy), cloned in the pP6 vector, transformed in *Saccharomyces cerevisiae*, Y187 strain, containing about 4 10⁶ independent clones, and a cell concentration about 5 10⁸ cells/ml.

In another aspect, the present invention relates to a collection of recombinant cell clones according to the invention, wherein the polynucleotide is inserted in the plasmid $pAS2\Delta\Delta$.

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Still another aspect, the present invention relates to a collection of recombinant cell clones according to the invention, wherein the polynucleotide is inserted in a plasmid selected from the group consisting of pT25, pKT25, pUT18 and pUT18C.

The present invention also relates to a kit for screening protein-protein interaction comprising a collection of recombinant cell clones usable for two-hybrid systems according to the invention.

In a particular embodiment of the collection according to the invention, the DNA library is presented as a ready to use kit for screening protein-protein interaction consisting in a collection of recombinant haploid yeast cells containing the whole genome as inserts generated during the construction of the DNA library under the form of prey polynucleotides, said collection of yeast cells being frozen in multiple vial containing an identical biological material.

The present invention also provides a generally method for selecting a polynucleotide of the collection according to the present invention, encoding a prey polypeptide, that is capable of interacting with bait polypeptide of interest.

As used interchangeably herein, the terms "polynucleotides", "nucleic acid" "oligonucleotides", include RNA, DNA, or RNA/DNA hybrid sequences of more than one nucleotide in either single chain or duplex form. The polynucleotide sequences of the invention may be prepared by any known method, including synthetic, recombinant, ex vivo generation, or a combination thereof, as well as utilizing any purification methods known in the art.

The term "purified" is used herein to describe a polynucleotide of the invention which has been separated from other compounds including, but not limited to other nucleic acids, carbohydrates, lipids and proteins. A polynucleotide is substantially pure when at least about 50 %, preferably 60 to 90 % weight/weight of a sample exhibits a single polynucleotide sequence, more usually about 95 %, and preferably is over about 99 %.

As used herein, the term "isolated" requires that the material be removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or DNA or polypeptide, separated from some or all of the coexisting materials in the natural system, is isolated. Such

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polynucleotide could be part of a vector and/or such polynucleotide or polypeptide could be part of a composition, and still be isolated in that the vector or composition is not part of its natural environment.

The term "polypeptide" refers to a polymer of amino acids without regard to the length of the polymer; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide, theses terms as used herein are interchangeable. The term "polypeptide" also does not specify or exclude post-expression modifications of polypeptides, for example, polypeptides which include the covalent attachment of glycosyl groups, acetyl groups, phosphate groups, lipid groups and the like are expressly encompassed by the term polypeptide. Also included within the definition are polypeptides which contain one or more analogs of an amino acid (including, for example, non-naturally occurring amino acids, amino acids which only occur naturally in an unrelated biological system, modified amino acids from mammalian).

The term "purified" is used herein to describe a polypeptide of the invention which has been separated from other compounds including, but not limited to nucleic acids, carbohydrates, lipids and other proteins. A purified polypeptide typically comprises about 50 %, preferably 60 to 90 % weight/weight of a protein sample, more usually about 95 %, and preferably is over about 99 % pure.

Bait polypeptide of interest is either a prokaryotic polypeptide encoded by a polynucleotide of the collection according to the present invention, or any other polypeptides of interest. Other polypeptides of interest can be polypeptides of an organism that may be infected by the prokaryotic micro-organism, for example, mammalian organism, in particular human organism.

The following described method is the mating yeast two-hybrid system and the bacterial two-hybrid system but variants of two-hybrid systems could also be used.

For example, the three hybrid system (Tirode et al., 1997, Journal of Biological Chemistry, 272, 22995-22999, A conditionally expressed third partner stabilises or prevents the formation of a transcriptional activator in a three-hybrid system) involves three polypeptides that allow or prevent the formation of the transcriptional activator. Beside the two-hybrid fusion proteins, the third partner is under the control of the Met25 promoter, which is positively regulated in medium lacking methionine. Another variant is the reverse two-hybrid system (Vidal et al., 1996, Proc. Natl. Sci., 93, 10315-

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10320, Reverse two-hybrid and one-hybrid system to detect dissociation of protein-protein and DNA-protein interaction) where a collection of molecules can be screened that may inhibit a specific protein-protein interaction.

Yet another aspect, the present invention relates to yeast two-hybrid system method for identifying a recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:

- a) mating at least one first haploid recombinant cell clone of a collection of recombinant cell clones according to the invention transformed with a plasmid containing the prey polynucleotide to be assayed with a second haploid recombinant S. cerevisiae cell clone transformed with a plasmid containing a bait polynucleotide encoding said bait polypeptide;
- b) cultivating diploid cell obtained in step a) on selective medium; and
- c) selecting recombinant cell clones capable of growing on selective medium.

In a particular embodiment, the invention is directed to a yeast two-hybrid system method for identifying a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:

- a) identifying a recombinant cell clone containing a prey polynucleotide encoding a
 prey polypeptide capable of interacting with a bait polypeptide according to the
 invention; and
- b) characterizing the prey polynucleotide contained in each recombinant cell clone selected in step a).

By yeast two-hybrid system is intended a method that usually makes use of at least one reporter gene, the transcription of which is activated when a prey polypeptide and a bait polypeptide produced by recombinant cell, due to the triggering of the transcription of said at least one reporter gene when both the specific domain contained in one prey polypeptide and the complementary domain contained in the bait polypeptide are in proximity one to the other. In an advantageous variant of yeast two hybrid system, prey polynucleotides encoding for prey polypeptides and bait polynucleotides encoding for bait polypeptides or proteins are inserted in recombinant haploid yeast cells, then a mating step leads to diploid yeast cells that produce the prey polypeptide and the bait polypeptide.

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By at least one reporter gene according to the invention, it is intended from one to five, and preferably two or three reporter genes, the transcription of which is activated within the recombinant diploid yeast cell when the encoded bait and prey polypeptide are capable of interacting.

Preferably, the at least one reporter gene is contained in the first recombinant haploid yeast cell containing the bait polynucleotide.

The at least one reporter gene may be contained either in a plasmid of the recombinant diploid yeast cell or in its genome.

As an illustrative embodiment, the at least one reporter gene is located in the chromosome of one recombinant haploid yeast cell used according to the previously described two-hybrid system and preferably the yeast cell containing the bait polynucleotide. The at least one reporter gene can be chosen among the group consisting in a nutritional gene or also a gene the expression of which is visualized by colorimetry, such as His3, LacZ or both LacZ and His3.

By "prey polynucleotide", it is intended a chimeric polynucleotide encoding a chimeric polypeptide comprising i) a specific domain and ii) a polypeptide that is to be tested for interaction with a bait polypeptide. The specific domain is preferably a transcriptional activating domain.

The prey polynucleotide may be obtained from a genomic library of a prokaryotic micro-organism, preferably from genomic DNA of *Helicobacter pylori*.

By a "bait polynucleotide", it is intended a chimeric polynucleotide encoding a chimeric polypeptide comprising i) a complementary domain and ii) a polypeptide that is to be tested for interaction with at least one prey polypeptide. The complementary domain is preferably a DNA-binding domain that recognizes a binding site on a detectable gene that is contained in a host organism.

Using as the bait polynucleotide, a complete open reading frame (ORF) that may be obtained either by digestion with a restriction endonuclease (Sambrook et al., 1973, Biochemistry 12(16): 3055-63 Detection of two restriction endonuclease activities in Haemophilus parainfluenzae using analytical agarose-ethidium bromide electrophoresis) or by digestion with an exonuclease such as Ball, or also by DNA synthesis. The complete ORF can also correspond to a given prey selected at given round with a two-hybrid system. An "open reading frame", also referred to herein as

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ORF, is a region of nucleic acid which encodes a polypeptide. This region may represent a portion of a coding sequence or a total sequence and be determined from a stop to stop codon or from a start to stop codon.

"DNA-binding domain" refers to a protein that specifically interacts with desoxyribonucleotide strands. A sequence-specific DNA binding protein binds to a specific sequence or family of specific sequences showing a high degree of sequence identity with each other.

The DNA binding domain of the bait polypeptide and the transcriptional activating domain of the prey polypeptide may be of different kinds. As an illustrative embodiment, these can be derived from LexA or also Gal4.

In one particular experiment of the yeast two-hybrid system, prey polypeptides are encoded by prey polynucleotides cloned in plasmid pACTIIst carrying Leu2 selection gene transformed in Y187 yeast cells carrying leucine auxotrophy and bait polypeptide are encoded by bait polynucleotide cloned in plasmid pAS2ΔΔ carrying Trp1 selection gene transformed in CG1945 yeast cells carrying tryptophane auxotrophy.

In another aspect, the present invention relates to a bacterial two-hybrid system method for identifying a recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:

- a) transforming bacterial cell clones with a plasmid containing a bait polynucleotide encoding said bait polypeptide;
- b) rescuing prey plasmids containing prey polynucleotides from the collection according to the present invention;
- c) transforming the recombinant bacterial cell clones obtained in step a) with the plasmid rescued in step b);
 - d) cultivating bacterial recombinant cells obtained in step c) on selective medium;
 - e) selecting recombinant cell clones capable of growing on selective medium.c) selecting recombinant cell clones capable of growing on selective medium.

In a preferred embodiment, the preparation of bacterial recombinant cells obtained in step c) of the bacterial two-hybrid system method for identifying a recombinant cell clone according to the invention comprises the following steps:

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- 1) E. coli is firstly transformed with bait plamid (standard protocol with chimio- or electro-competent cells);
- 2) prey plasmids are rescued from collection according to the invention (prey plasmids are in *E. coli* bacterial strain, cf. protocol 1.B « the plasmid DNA contained in E. coli are extracted (Qiagen) from aloquoted E. coli frozen cells »);
- 3) rescued prey plasmids are then transformed in recombinant *E coli* of step 1 according to standard protocols of transformation (for example using electro- of chimio-competent cells).

In a particular embodiment, the invention is directed to a bacterial two-hybrid system method for identifying a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:

- a) identifying a recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide according to the invention; and
- b) characterizing the prey polynucleotide contained in each recombinant cell clone selected in step a).

By bacterial two-hybrid system is intended a method that usually makes use of at least one reporter gene, the transcription of which is activated when a prey polypeptide and a bait polypeptide produced by recombinant cell, due to the triggering of the transcription of said at least one reporter gene when both the specific domain contained in one prey polypeptide and the complementary domain contained in the bait polypeptide are in proximity one to the other.

In a particular embodiment of the bacterial two-hybrid system, specific domain of prey polypeptide and complementary domain of bait polypeptide are part of the catalytic domain of an enzyme. Interaction of prey polypeptide and bait polypeptide allows restoration of enzyme catalytic domain and, as a consequence, to the restoration of the enzyme activity.

In a more preferred embodiment of the bacterial two-hybrid method, enzyme is Bordetella *pertussis* adenylate cyclase which activation, via proximity of T25 and T18 fragments of the catabolic domain, leads to cAMP synthesis, cAMP then triggers transcriptional activation of catabolic operons, such as lactose or maltose.

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Still another aspect, the present invention relates to a method according to the invention, wherein the bait polypeptide and the prey polypeptide (encoded by a polynucleotide inserted in cell clone from the collection according to the present invention) are originating from the same prokaryotic micro-organism, particularly from Helicobacter pylori, Escherichia coli, Staphylococcus aureus or Streptococcus pneumoniae or wherein the bait polypeptide is originating from a human polypeptide and the prey polypeptide is originating from a prokaryotic micro-organism, particularly from Helicobacter pylori.

Yet another aspect, the present invention relates to a recombinant diploid yeast cell obtained by step a) of the yeast two-hybrid system method for identifying a recombinant cell clone according to the invention as described above.

The recombinant diploid yeast cell obtained by the the yeast two-hybrid system method for identifying a recombinant cell clone according to the invention, also forms part of the present invention.

By performing yeast or bacterial two-hybrid system, it can be possible to identify for one particular bait interacting prey polypeptide. Prey polynucleotide that has been selected by testing the collection in a screening two-hybrid method encodes for polypeptide interacting with a protein of interest.

The running of the two-hybrid method leads to the identification of interactions between prokaryotic prokaryotic polypeptides, especially *Helicobacter pylori*, *Escherichia coli*, *Staphylococcus aureus* or *Streptococcus pneumoniae* polypeptides, or eukaryotic-prokaryotic polypeptides, these interactions are also part of the invention.

In another aspect, the present invention is directed to a polynucleotide, or fragment thereof, encoding a prey polypeptide capable of interacting with a bait polypeptide wherein said polynucleotide is identified by a method according to the invention.

In a preferred embodiment, the invention comprises the polynucleotides according to the invention, selected from the group consisting of:

 a) a polynucleotide having the nucleic acid sequence of an ORF identified by the reference indicated in the right column "interacting ORF" in table I, and fragment thereof having at least 12 consecutive nucleotides;

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- b) a polynucleotide having at least 80 %, preferably at least 85 %, 90 %, 95 % and 99 %, nucleotides identity degree after alignment to a nucleic acid sequence of a polynucleotide of a);
- c) a polynucleotide comprising the nucleic acid sequence of a polynucleotide of a) or b).

Still another aspect, the present invention is directed to a polynucleotide, or fragment thereof, encoding a bait polypeptide capable of interacting with a prey polypeptide wherein the polynucleotide encoding said prey polypeptide is identified by a method according to the invention.

In a preferred embodiment, the invention comprises the polynucleotides according to the invention, selected from the group consisting of:

- a) a polynucleotide having the nucleic acid sequence of an ORF identified by the reference indicated in the left column "bait polypeptide" in table I, and fragment thereof having at least 12 consecutive nucleotides;
- b) a polynucleotide having at least 80 %, preferably at least 85 %, 90 %, 95 % and 99 %, identity degree after alignment to a nucleic acid sequence of a polynucleotide of a);
 - c) a polynucleotide comprising the nucleic acid sequence of a polynucleotide of a) or b).

Yet another aspect, the present invention relates to a set of two polynucleotides consisting of a first polynucleotide, or fragment thereof, encoding a prey polypeptide capable of interacting with a bait polypeptide according to the invention and a second polynucleotide, or a fragment thereof having at least 12 consecutive nucleotides, encoding said bait polypeptide.

The polypeptides encoded by the polynucleotides according to the invention and the sets of two polypeptides encoded by the sets of two polynucleotides according to the invention, also form part of the invention.

In a preferred embodiment, the invention concerns an isolated complex comprising at least the two polypeptides encoded by a set of two polynucleotides according to the invention, preferably said two polypeptides are associated in the complex by affinity binding.

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In a preferred embodiment, the invention concerns an isolated complex comprising at least a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP1293 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In a preferred embodiment, the invention concerns an isolated complex comprising at least a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP0088 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In a preferred embodiment, the invention concerns an isolated complex comprising at least a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP1032 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In another aspect, the present invention relates to a protein-protein interaction wherein the two interacting proteins consist of a set of two polypeptides according to the invention.

In a preferred embodiment, the invention relates to the protein-protein interactions according to the invention, wherein the sets of two polypeptides consist of two Helicobacter pylori, Escherichia coli, Staphylococcus aureus or Streptococcus pneumoniae polypeptides.

When several reiterations of the two-hybrid method are performed and thus common bait and prey polypeptide are selected, a map of all the interactions between these polypeptides may be designed, that take into account of the known and/or suspected biological function of each of the interacting polypeptides.

Such an Proteins Interaction Map (PIM®) may help the one skilled in the art to decipher a whole metabolical and/or physiological pathway that is functionally active

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within the host organism from which the initial DNA library is derived. Protein Interaction Map and computable version of PIM® are part of the present invention.

Therefore still another aspect, the present invention is directed to a computable readable medium (such as floppy disk, diskette, CD-rom, and all electronic or magnetic format which can be read by a computer) having stored thereon protein-protein interactions according to the invention, preferably stored in a form of a protein interaction map, as showed, for example, in Fromont-Racine et al., Nature Genetics, 1997, Letter, 277-281, figure 3, page 279.

In a preferred embodiment, the invention comprises a computable readable medium according to the invention, wherein the protein-protein interactions stored thereon are linked to annotated database, for example through Internet.

In an other preferred embodiment, the invention comprises a data bank containing the protein-protein interactions stored thereon, said databank being avalaible on a World-Wide Web site, said databank may be annoted by means of others databank.

As the source genomic DNA is randomly fragmented before being inserted in recombinant vectors, several prey polypeptides may be selected for one bait polypeptide. Therefore it is possible to define the Selected Interacting Domain (SID®) which contains the precise polypeptide domain involved in the interaction between the prey polypeptide and the bait polypeptide.

So, in another aspect, the invention relates to a method for identifying a polynucleotide encoding a selected interacting domain (SID®) of a prey polypeptide of interest from a prokaryotic micro-organism capable of interacting with a bait polypeptide comprising the steps of:

- a) selecting from prey polynucleotides identifying by a method according to the invention all prey polynucleotides encoding a polypeptide capable of interacting with said bait polypeptide and containing a nucleic acid fragment identical to a nucleic fragment of the polynucleotide encoding the prey polypeptide of interest;
- b) determining the polynucleotide common to said all prey polynucleotides selected in step a); and
- c) identifying the polynucleotide determining in step b) as being the polynucleotide encoding the selected interacting domain (SID®) of said prey polypeptide of interest.

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The polynucleotides encoding a selected interacting domain (SID®) of a prey polypeptide of interest from a prokaryotic micro-organism capable of interacting with a bait polypeptide obtainable by this method, also form part of the invention.

In a particular embodiment, the prey polypeptide of interest is originating from Helicobacter pylori, Escherichia coli, Staphylococcus aureus or Streptococcus pneumoniae.

In a preferred embodiment, the polynucleotides encoding a selected interacting domain (SID®) of a prey polypeptide of interest according to the invention are selected from the group consisting of:

- a) a polynucleotide encoding an amino acids sequence identified by the reference indicated in the right column "SID®" in table II;
 - b) a polynucleotide having the sequence identified by the reference indicated in the right column "SID®" in table III;
 - c) fragment having at least 12, 15, 25 or 50 consecutive nucleotides of polynucleotide of a) or b), complement thereof, and RNA corresponding to said polynucleotide; and
 - d) a polynucleotide having at least 80 %, preferably 85 %, 90 %, 95 % and 99 %, identity degree after alignment to a nucleic acid sequence of a polynucleotide of a) or b).

The term "complement thereof" are used herein to refer to the sequences of polynucleotides which is capable of forming Watson & Crick base pairing with another specified polynucleotide throughout the entirety of the complementary region. This term is applied to pairs of polynucleotides based solely upon their sequences and not any particular set of conditions under which the two polynucleotides would actually bind.

The term "degree of sequence identity" is used herein to refer to comparisons among polynucleotides and polypeptides, and are determined by comparing two optimally aligned sequences over a comparison window, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e., gaps) as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid base or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of

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positions in the window of comparison and multiplying the result by 100 to yield the percentage of sequence identity. Homology is evaluated using any of the variety of sequence comparison algorithms and programs known in the art. Such algorithms and programs include, but are by no means limited to BLASTN, BLASTP (Altschul et al., 1990, J. Mol. Biol. 215(3): 403-410 / Altschul et al., 1993, Nature Genetics 3:266-272 / Altschul et al., 1997, Nuc. Acids Res. 25:3389-3402).

The definition of sequence identity given above is the definition that would use one of skill in the art. The definition by itself does not need the help of any algorithm, said algorithms being helpful only to achieve the optimal alignments of sequences, rather than the calculation of sequence identity.

From the definition given above, it follows that there is a well defined and only one value for the sequence identity between two compared sequences which value corresponds to the value obtained for the best or optimal alignement.

In the BLAST N or BLAST P "BLAST 2 sequence" (Tatusova et al., Blast 2 sequences - a new tool for comparing protein and nucleotide sequences, FEMS Microbiol. Lett. 174: 247-250) software which is available in the web site http://www.ncbi.nlm.nih.gov/gorf/bl2.html, and habitually used by the inventors and in general by the skilled man for comparing and determining the identity between two sequences, the "open gap penaltie" and « extension gap penaltie » parameters which depend on the substitution matrix selected regarding the nature and the length of the sequence to be compared are directly selected by the software (i.e "5" and "2" respectively for substitution matrix BLOSUM-62). The identity percentage between the two sequences to be compared is directly calculated by the software.

In another object, the invention also comprises the polypeptides selected from the group consisting of:

- a) a polypeptide having an amino acids sequence identified by the reference indicated in the right column "SID®" in table II, and fragment thereof having at least 5 consecutive amino acids; and
- b) a polypeptide encoded by a polynucleotide encoding a selected interacting domain (SID®) of a prey polypeptide of interest according to the invention.

Still another aspect, the invention relates to the use of a polynucleotide according to the present invention as a primer or a probe for the amplification and/or the

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detection of polynucleotide encoded a prey polypeptide of interest, or its SID®, capable of interacting with a bait polypeptide according to the present invention.

In another aspect, the present invention concerns cloning or expression vector containing a polynucleotide according to the invention.

Particularly preferred vectors of the invention include the plasmid pACTIIst, pAS2ΔΔ, pP6 or the plasmid selected from the group consisting of pT25, pKT25, pUT18 and pUT18C.

Further preferred vectors are self replicated or viral vectors, such as adenovirus, AAV, a retrovirus, a poxvirus or an herpes virus.

The vectors according to the invention, characterized in that they comprise the elements allowing the expression and/or the secretion of the said sequences in a host cell, also form part of the invention.

Vector according to the invention including elements allowing expression and/or secretion of said polynucleotide in a host cell also form part of the invention.

The vectors according to the invention characterized in that they comprise a promoter and/or regulator sequence, or a sequence for cellular addressing according to the invention, or one of their fragments, are also included in the invention.

The said vectors will preferably comprise a promoter, signals for initiation and termination of translation, as well as appropriate regions for regulation of transcription. They may also be capable of being stably maintained in the cell and may optionally possess particular signals specifying the secretion of the translated protein.

These different control signals are chosen according to the cellular host used. To this end, the nucleic acid sequences according to the invention may be inserted into autonomously replicating vectors inside the chosen host, or integrative vectors of the chosen host.

Among the autonomously or self replicating systems, there will be preferably used according to the host cell, systems of the plasmid or viral type, it being possible for the viral vectors to be in particular adenoviruses (Perricaudet et al., 1992, La Recherche 23: 471-473, 1992), retroviruses, poxviruses or herpes viruses (Epstein et al., 1992, Médecine/Sciences 8: 902-911, 1992). Persons skilled in the art know the technologies which can be used for each of these systems.

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When the integration of the sequence into the chromosomes of the host cell is desired, it will be possible to use, for example, systems of the plasmid or viral type; such viruses will be, for example, retroviruses (Temin, 1986, In Kucherlapati R., ed. Gene Transfer, New York, Plenum Press, 149-187, 1986), or AAVs (Carter, 1993, Curr. Op. Biotechnology 3: 533-539, 1993).

Such vectors will be prepared according to the methods commonly used by persons skilled in the art, and the clones resulting therefrom may be introduced into an appropriate host by standard methods such as, for example, lipofection, electroporation or heat shock.

The invention comprises, in addition, the host cells, in particular eukaryotic and prokaryotic cells, transformed by the vectors according to the invention.

Among the cells which can be used for these purposes, there may of course be mentioned bacterial cells (Olins et al., Curr. Op. Biotechnology 4: 520-525, 1993), but also yeast cells (Buckholz, Curr. Op. Biotechnology 4: 538-542, 1993), as well as animal cells, in particular mammalian cell cultures (Edwards and Aruffo, Curr. Op. Biotechnology 4: 558-563, 1993), and in particular Chinese hamster ovary cells (CHO), but also insect cells in which it is possible to use methods using baculoviruses, for example (Luckow et al., Curr. Op. Biotechnology 4: 564-572, 1993). A preferred cellular host for the expression of the proteins of the invention consists of the CHO cells.

The cells according to the invention can be used in a method for the production of a polypeptide according to the invention, as described below, and can also serve as a model for analysis and screening.

So, the present invention comprises a method for producing a polypeptide of the invention comprising the steps of:

- a) cultivating a host cell according to the invention under conditions and in culture medium allowing the growth of said host cell and the expression of said polypeptide; and
- b) recovering said polypeptide directly from the culture medium or from said cultivated cell obtained in step a).

Recombinant polypeptide obtained by the method above also form part of the invention.

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The term "recombinant polypeptide" is used herein to refer to polypeptides that have been artificially designed and which comprise at least two polypeptide sequences that are not found as contiguous polypeptide sequences in their initial natural environment, or to refer to polypeptides which have been expressed from a recombinant polynucleotide.

The method for the production of a polypeptide of the invention in recombinant form is itself included in the present invention, and is characterized in that the transformed cells, are cultured under conditions allowing the expression of a recombinant polypeptide encoded by a polynucleotide according to the invention, and in that the said recombinant polypeptide is recovered.

Also forming part of the invention is a method for the production of a heterologous polypeptide, characterized in that it uses a vector or a host cell according to the invention.

The recombinant polypeptides, characterized in that they are obtainable by the said method of production, also form part of the invention.

The recombinant polypeptides obtained as indicated above may be both in glycosylated and non-glycosylated form and may or may not have the natural tertiary structure.

These polypeptides may be produced from the polynucleotide, according to techniques for the production of recombinant polypeptides known to persons skilled in the art. In this case, the polynucleotide used is placed under the control of signals allowing its expression in a cellular host.

An effective system of production of a recombinant polypeptide requires having a vector and a host cell according to the invention.

These cells may be obtained by introducing into the host cells a nucleotide sequence inserted into a vector as defined above, and then culturing the said cells under conditions allowing the replication and/or expression of the transfected nucleotide sequence.

The methods for the purification of a recombinant polypeptide which are used are known to persons skilled in the art. The recombinant polypeptide may be purified from cell lysates and extracts, from the culture medium supernatant, by methods used individually or in combination, such as fractionation, chromatographic methods,

immunoaffinity techniques with the aid of specific mono- or polyclonal antibodies, and the like.

A preferred variant consists in producing a recombinant polypeptide fused with a "carrier" protein (chimeric protein). The advantage of this system is that it allows a stabilization and a reduction in proteolysis of the recombinant product, an increase in solubility during in vitro renaturation and/or simplification of the purification when the fusion partner has affinity for a specific ligand.

The invention also relates to the synthesis of synthetic polypeptides of the invention, in particular by chemical synthesis.

The polypeptides according to the present invention can be obtained by chemical synthesis using any of the numerous known peptide syntheses, for example the techniques using solid phases or techniques using partial solid phases, by condensation of fragments or by a conventional synthesis in solution.

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Also forming part of the invention are the methods for the determination of the presence of a polynucleotide or a polypeptide encoded by involved in an protein-protein interaction of the present invention, characterized in that they use a polynucleotide or an antibody according to the invention.

These methods relate to, for example, the methods for the diagnosis *in vitro* of the presence in a biological sample of the procaryotic micro-organism from which said polypeptide is originating. The polynucleotide analysed may be either the genomic DNA, the cDNA or the mRNA.

These methods can use the probes and primers of the present invention.

The term "primer" denotes a specific oligonucleotide sequence which is complementary to a target nucleotide sequence and used to hybridize to the target nucleotide sequence. A primer serves as an initiation point for nucleotide polymerization catalyzed by either DNA polymerase, RNA polymerase or reverse transcriptase.

The term "probe" denotes a defined nucleic acid segment (or nucleotide analog segment, e.g., polynucleotide as defined hereinbelow) which can be used to identify a specific polynucleotide sequence present in samples, said nucleic acid segment comprising a nucleotide sequence complementary of the specific polynucleotide sequence to be identified.

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They are generally purified nucleic sequences for hybridization comprising at least 12 nucleotides, preferably at least 15, 20 and 25 nucleotides, characterized in that they can hybridize specifically with the polynucleotide chosen encoding the polypeptide of interest involved in an protein-protein interaction of the present invention.

Among the methods for the determination of the presence of a polynucleotide encoding a polypeptide of interest involved in an protein-protein interaction of the present invention, the methods comprising at least one stage for the so-called PCR (polymerase chain reaction) or PCR-like amplification of the target polynucleotide according to the invention with the aid of a pair of primers of nucleotide sequences according to the invention are preferred.

PCR-like will be understood to mean all methods using direct or indirect reproductions of nucleic acid sequences, or alternatively in which the labelling systems have been amplified, these techniques are of course known, in general they involve the amplification of DNA by a polymerase; when the original sample is an RNA, it is advisable to carry out a reverse transcription beforehand. There are currently a great number of methods allowing this amplification, for example the so-called NASBA "Nucleic Acid Sequence Based Amplification" (Compton J. 1991 Nature. 350 (6313): 91-92), TAS "Transcription based Amplification System" (Guatelli et al., 1990, Proc. Natl. Acad. Sci. USA. 35: 273-286), LCR "Ligase Chain Reaction" (Landegren et al., 1998, Genome Research, 8:769-776), "Endo Run Amplification" (ERA), "Cycling Probe Reaction" (CPR), and SDA "Strand Displacement Amplification" (Walker et al., Nucleic Acids Res. 20: 1691-1696, 1992), methods well known to persons skilled in the art.

The invention comprises, in addition, methods for the determination of the presence of a polypeptide of interest involved in an protein-protein interaction of the present invention, characterized in that an antibody according to the invention is brought into contact with the biological material to be tested, under conditions allowing the possible formation of specific immunological complexes between the said polypeptide and the said antibody, and in that the immuno-logical complexes possibly formed are detected, such as, for example, methods using RIA or ELISA.

The transformed cells as described above can also be used as models so as to study the interactions between a polypeptide of the invention and their interacting

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partners polypeptide, or between a polypeptide of the invention and chemical or protein compounds which are capable of modulating the protein-protein interaction according to the invention wherein said polypeptide of the invention is involved.

In particular, they may be used for the selection of products which interact with a polypeptide of the invention, or one of its SID® domains, as cofactor or as inhibitor, in particular a competitive inhibitor, or alternatively having an agonist or antagonist activity on the protein-protein interaction wherein said polypeptide of the invention is involved. Preferably, the said transformed cells will be used as a model allowing, in particular, the selection of products which make it possible to prevent and/or to treat pathologies induced by prokaryotic micro-organism.

Still another aspect of the invention pertains to a method for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides according to the invention comprising the steps of:

- a) cultivating a recombinant cell clone containing a reporter gene expression of which is toxic for said recombinant cell clone and transformed with two plasmids wherein:
 - i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and a DNA binding domain;
 - ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and an activating domain capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting;

on a selective medium containing the agent to be tested and allowing the growth of said recombinant cell clone when the toxic reporter gene is not activated; and

b) selecting agent which is capable of inhibiting the growth of the recombinant cell clone cultivated in step a).

The invention also comprises a method for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides according to the invention comprising the steps of:

a) cultivating a recombinant cell clone, preferably permeable, containing a reporter gene expression of which is toxic for said recombinant cell clone and transformed with two plasmids wherein:

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- i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and the first domain of an enzyme;
- ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and the second part of said enzyme capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting, said interaction restoring the activity of the enzyme;

on a selective medium containing the agent to be tested and allowing the growth of said recombinant cell clone when the toxic reporter gene is not activated; and

b) selecting agent which is capable of inhibiting the growth of the recombinant cell clone cultivated in step a).

In a preferred embodiment, said toxic reporter gene that can be used for negative selection, is URA3, CYH1 or CYH2 gene.

Still another aspect of the invention pertains to a method for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides according to the invention comprising the steps of:

- a) cultivating a recombinant cell clone containing a reporter gene expression of which stimulates the growth of said recombinant cell clone and transformed with two plasmids wherein:
 - i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and a DNA binding domain;
 - ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and an activating domain capable of activating said stimulating reporter gene when the first and the second hybrid polypeptides are interacting;

on a selective medium containing the agent to be tested and allowing the normal growth of said recombinant cell clone when the stimulating reporter gene is not activated; and

b) selecting agent which is capable of stimulating the growth of the recombinant cell clone cultivated in step a).

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In a preferred embodiment, the method according to the invention for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides is a method for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP1293 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In a preferred embodiment, the method according to the invention for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides is a method for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP0088 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In a preferred embodiment, the method according to the invention for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides is a method for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP1032 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In another embodiment of the invention, inventors provide a kit for screening a modulator agent comprising at least one recombinant diploid clone or a cell clone, haploid or diploid, transformed with a plasmid containing a sequence coding for a bait polypeptide and a plasmid containing the nucleotide sequence of a SID® or of homologue polypeptide of SID®, said plasmids may be chosen between pACTIIst and pAS2ΔΔ.

SID® or homologue sequence of SID® acting on the same pair of interacting proteins may be also modulator agents.

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Modulator agent selected by anyone of the yeast or bacterial two-hybrid system method of the invention also forms part of the invention.

These modulator agents of protein-protein interaction according to the invention may be obtained for example from a library of compounds.

Consequently, is also part of the invention a modulator agent selected by the method of the invention previously described capable of interfering with a protein-protein interaction according to the invention. This agent may modulate an interaction of the invention between two prokaryotic polypeptides, particularly between two Helicobacter pylori, Escherichia coli, Staphylococcus aureus or Streptococcus pneumoniae polypeptides, or between a prokaryotic polypeptide, such as Helicobacter pylori, Staphylococcus aureus or Streptococcus pneumoniae polypeptide, and a polypeptide originating from a host organism of said prokaryotic micro-organism, such as mammal, particularly human.

These methods allow the selection of chemical or biochemical compound capable of interacting, directly or indirectly, with the polynucleotide or the polypeptide encoded by of the invention, in particular capable of modulating the protein-protein interaction wherein said polypeptide of the invention is involved.

More particularly, the invention concerns modulator agent capable of modulating, more preferred of inhibiting, the viability and/or the growth of the prokaryotic micro-organism, preferrably *Helicobacter pylori*, *Staphylococcus aureus* or *Streptococcus pneumoniae*, from which is the protein-protein interaction.

For the screening of compounds capable of modulating the protein-protein interaction wherein said polypeptide of the invention is involved, the preferred principal effect is the effect of inhibiting the viability and/or the growth of the prokaryotic microorganism, preferrably *Helicobacter pylori*, *Staphylococcus aureus* or *Streptococcus pneumoniae*, from which is the protein-protein interaction.

These effects of modulating the viability and/or the growth of prokaryotic microorganisms can be analysed by any method known by a skilled man.

For example, a screening method of modulating agent can comprise the following steps:

- Select one specific interaction.

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- Transform a permeabilized yeast cell with plasmids containing bait polypeptide and prey polypeptide of the specific interaction.
- Plate a top agar containing transformed permeabilized yeast cells on square boxes (that already contains agarose gel).
 - Apply by spotting the compounds to test on top agar as soon as it is solidified.
 - Incubate, for example overnight at 30°C, and
- Analyse results : select lead compounds that prevent transformed permeabilized yeast cells from growing.

Screening may be used to test compounds capable of modifying the level and/or the specificity of expression of the polynucleotide or the polypeptide encoded by of the invention involved in the protein-protein interaction according to the invention.

A quantitative or qualitative analysis of the expression of the gene encoded the polypeptide of the invention involved in the protein-protein interaction according to the invention can be carried out using primers or probes of the invention as DNA templates, the term DNA templates designating nucleic acids having a sufficient length to allow a specific detection of the expression of mRNAs capable of hybridizing thereto. For example, the DNA templates contain nucleic acids derived from said gene, or sequences complementary thereto for which it is desired to estimate the level or the specificity of expression, and comprising at least 15, at least 25, at least 50, at least 100 or at least 500 consecutive nucleotides.

Another aspect of the present invention consists in methods of identifying molecules capable of binding to one of the set of two polypeptides of the invention involved in the protein-protein interaction. Such molecules can be used to modulate the viability and/or the growth of the prokaryotic micro-organism, preferrably *Helicobacter pylori*, from which is the protein-protein interaction activity. For example, such molecules can be used to stimulate or to inhibit a biological reaction involved in the viability and/or the growth of the prokaryotic micro-organism.

Numerous methods well known by the skilled man exist for identifying ligands for a defined polypeptide.

For example to identifying molecules capable of binding to one polypeptide of the set of two polypeptides of the invention involved in the protein-protein interaction, a subunit thereof or a fragment thereof comprising at least 10, at least 20, at least 30, or

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more than 30 consecutive amino acids with small molecules such as those generated by combinatory chemistry, it is possible to use an HPLC-coupled microdialysis, or an affinity capillary electrophoresis.

In other methods, the peptides or small molecules capable of interacting with said one of the set of two polypeptides of the invention, a subunit thereof or a fragment thereof may be linked to detectable markers such as radioactive, fluorescent or enzymatic markers. These labelled molecules are brought into contact with the immobilized said one of the set of two polypeptides of the invention, under conditions allowing a specific interaction. After elimination of the molecules which are not specifically bound, the bound molecules are detected by appropriate means.

In addition, the peptides or small molecules which bind to said one of the set of two polypeptides of the invention, preferably to its SID® binding site can be identified by competition experiments. In such experiments, said one of the set of two polypeptides of the invention, is immobilized on a surface. Increasing quantities of peptides or of small molecules are brought into contact with the immobilized said one of the set of two polypeptides of the invention in the presence of the second labelled polypeptide of said two polypeptides of the invention, designated labelled ligand. The labelled ligand may be labelled with a radioactive, fluorescent or enzymatic marker. The capacity of the molecule tested to interact with said one of the set of two polypeptides of the invention is determined by measuring the quantity of labelled ligand bound in the presence of the molecule tested. A decrease in the quantity of bound ligand when the molecule tested is present indicates that the latter is capable of interacting with said one of the set of two polypeptides of the invention.

The Biacore™ technology can also be used to carry out the screening of compounds capable of interacting with said one of the set of two polypeptides of the invention. This technology is described in Szabo et al. (1995) and in Edwards and Leartherbarrow (Analytical Biochemistry, 246, 1-6, 1997), of which the teaching is incorporated by reference, and makes it possible to detect interactions between molecules in real time without the use of labelling.

One of the main advantages of this method is that it allows the determination of the association constants between said one of the set of two polypeptides of the invention and the interacting molecules. Thus, it is possible to specifically select the molecules interacting with high or low association constants.

The proteins or other molecules interacting said one of the set of two polypeptides of the invention can be identified using affinity columns which contain said one of the set of two polypeptides of the invention. Said one of the set of two polypeptides of the invention may be attached to the column using conventional techniques including chemical coupling to an appropriate column matrix such as agarose, Affi Gel, or other matrices known to a person skilled in the art. In another aspect of the invention, the affinity column may contain chimeric proteins in which said one of the set of two polypeptides of the invention would be fused, for example, with glutathione S-transferase. The molecules to be tested which are described above are then deposited on the column. The molecules interacting said one of the set of two polypeptides of the invention are retained by the column and can be isolated by elution.

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The chemical or biochemical compounds, characterized in that they make it possible to modulate, directly or indirectly, the protein-protein interaction according to the invention, and selected by the said methods defined above, also form part of the invention.

The use of a polypeptide according to the invention for the modulation of *Helicobacter pylori*'s protein interaction, also forms part of the present invention.

Still another aspect, the present invention is directed to a method for the production of monoclonal or polyclonal antibodies comprising the step of immunization of an animal or human organism with an immunogenic agent comprising a polypeptide, a vector according or a host cell according to the invention, and to antibodies obtained by said method.

The mono- or polyclonal antibodies or fragments thereof, chimeric or immunoconjugated antibodies, characterized in that they are capable of specifically recognizing a polypeptide according to the invention, also form part of the invention.

As used herein, the term "antibody" refers to a polypeptide or group of polypeptides which are comprised of at least one binding domain, where an antibody binding domain is formed from the folding of variable domains of an antibody molecule to form three-dimensional binding spaces with an internal surface shape and charge distribution complementary to the features of an antigenic determinant of an antigen,

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which allows an immunological reaction with the antigen. Antibodies include recombinant proteins comprising the binding domains, as wells as fragments, including Fab, Fab', F(ab)2, and F(ab')2 fragments.

Specific polyclonal antibodies may be obtained from a serum of an animal immunized against a polypeptide according to the invention, in particular produced by genetic recombination or by peptide synthesis, according to the customary procedures, from a polynucleotide according to the invention.

The specific monoclonal antibodies may be obtained according to the conventional hybridoma culture method described by Kohler and Milstein (Kohler, G. and Milstein, C., Nature 256:495, 1975).

The antibodies according to the invention are, for example, chimeric antibodies, humanized antibodies, Fab or F(ab')2 fragments. They may also be in the form of immunoconjugates or of labelled antibodies so as to obtain a detectable and/or quantifiable signal (Harlow, E., and D. Lane. 1988. Antibodies A Laboratory Manual. Cold Spring Harbor Laboratory. pp. 53-242).

The invention also relates to methods for the detection and/or purification of a polypeptide according to the invention, characterized in that they use an antibody according to the invention.

The invention comprises, in addition, purified polypeptides, characterized in that they are obtained by a method according to the invention.

Moreover, in addition to their use for the purification of polypeptides, the antibodies of the invention, in particular the monoclonal antibodies, may also be used for the detection of these polypeptides in a biological sample.

They thus constitute a means for the immunocytochemical or immunohistochemical analysis of the expression of polypeptide against which they are raised on specific tissue sections, for example by immunofluorescence, gold labelling, enzymatic immunoconjugates.

They make it possible in particular to detect expression of these polypeptides in the biological tissues or samples, which makes them useful for monitoring the progress of a method of prevention or treatment.

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More generally, the antibodies of the invention may be advantageously used in any situation where the expression of a polypeptide of the invention against which they are raised needs to be observed.

The invention finally relates to a polynucleotide, a polypeptide, a vector, a host cell, a modulator agent or an antibody to the invention as compound for the preparation of a medicament.

So the invention also encompasses a pharmaceutical composition comprising a compound selected from the group consisting of:

- a) a polynucleotide according to the invention;
- 10 b) a polypeptide according to the invention;
 - c) a vector according to the invention;
 - d) a host cell according to the invention;
 - e) a modulator agent to the invention; and
 - f) an antibody to the invention.

A pharmaceutical composition according to the invention, wherein said composition is administered by any route such as intravenous route, intramuscular route, oral route, or mucosal route with an acceptable physiological carrier and/or adjuvant, also forms part of the invention.

The compounds according to the invention as a medicament for the prevention and/or treatment of pathologies of infection diseases induced by prokaryotic microorganism are particularly preferred.

The most preferred are the compounds according to the invention, as a medicament for the prevention and/or treatment of infection diseases induced by Helicobacter pylori, Staphylococcus aureus or Streptococcus pneumoniae.

The compounds of the invention as active ingredients of a medicament will be preferably in soluble form, combined with a pharmaceutically acceptable vehicle.

Such compounds which can be used as a medicament offer a new approach for preventing and/or treating pathologies linked to infection by prokaryotic microorganism such as *Helicobacter pylori*, *Staphylococcus aureus* or *Streptococcus pneumoniae*. Preferably, these compounds will be administered by the systemic route, in particular by the intravenous route, by the intramuscular or intradermal route or by the oral route.

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Their modes of administration, optimum dosages and galenic forms can be determined according to the criteria generally taken into account in establishing a treatment suited to a patient, such as for example the age or body weight of the patient, the seriousness of his general condition, the tolerance to treatment and the side effects observed, and the like.

The identified compounds can be administered to a mammal, including a human patient, alone or in pharmaceutical compositions where they are mixed with suitable carriers or excipient(s) at therapeutically effective doses to treat disorders associated with prokaryotic micro-organism infection. Techniques for formulation and administration of the compounds of the instant application may be found in "Remington's Pharmaceutical Sciences", Mack Publishing Co., Easton, PA, latest edition.

Suitable routes of administration include oral, rectal, transmucosal, or intestinal administration, parenteral delivery, including intramuscular, subcutaneous, injections, as well as intravenous, intraperitoneal or intranasal injections.

Pharmaceutical compositions and medicaments for use in accordance with the present invention may be formulated in a conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries. Proper formulation is dependent upon the route of administration chosen.

For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer such as a phosphate or bicarbonate buffer. For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with fillers such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added. All

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formulations for oral administration should be in dosages suitable for such administration.

For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

For administration by inhalation, the compounds for use according to the present invention are conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebulizer, with the use of a suitable gaseous propellant, e.g., carbon dioxide. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, e.g., gelatin, for use in an inhaler or insufflator, may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

The compounds may be formulated for parenteral administration by injection, e.g., by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, e.g., in ampoules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Aqueous suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

Alternatively, the active ingredient may be in powder or lyophilized form for constitution with a suitable vehicle, such as sterile pyrogen-free water, before use.

Additionally, the compounds may be delivered using a sustained-release system, such as semipermeable matrices of solid hydrophobic polymers containing the therapeutic agent. Various sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature, release the compounds for a few weeks up to over 100 days.

Depending on the chemical nature and the biological stability of the therapeutic reagent, additional strategies for protein stabilization may be employed.

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The pharmaceutical compositions also may comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include but are not limited to calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols.

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective amount to achieve their intended purpose. More specifically, a therapeutically effective amount means an amount effective to prevent development of or to alleviate the existing symptoms of the subject being treated. Determination of the effective amounts is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein.

For any compound used in the method of the invention, the therapeutically effective dose can be estimated initially from cell culture assays. For example, a dose can be formulated in animal models to achieve a circulating concentration range that includes or encompasses a concentration point or range shown the desired effect in an in vitro system. Such information can be used to more accurately determine useful doses in humans.

A therapeutically effective dose refers to that amount of the compound that results in amelioration of symptoms in a patient. Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD50, (the dose lethal to 50 % of the test population) and the ED50 (the dose therapeutically effective in 50 % of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio between LD50 and ED50. Compounds which exhibit high therapeutic indices are preferred.

The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in human. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED50, with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the

patient's condition (see, e.g., Fingl et al., 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1).

Dosage amount and interval may be adjusted individually to provide plasma levels of the active compound which are sufficient to maintain the modulating effects. Dosages necessary to achieve the modulating effect will depend on individual characteristics and route of administration.

The amount of composition administered will, of course, be dependent on the subject being treated, on the subject's weight, the severity of the affliction, the manner of administration and the judgment of the prescribing physician.

Other characteristics and advantages of the invention appear in the remainder of the description with the examples and figures whose legends are represented below.

Examples

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Medium composition and standard protocols are available in Sambrook and Maniatis (Sambrook, J., Fritsch, E.F., and T. Maniatis. (1989) Molecular Cloning: A Laboratory Manual. 2ed. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York).

Example 1: Preparation of a Helicobacter pylori genomic collection

1.A. Collection preparation and transformation in Escherichia coli

1.A.1. Fragmented of genomic DNA preparation

The *Helicobacter pylori* genomic DNA is fragmented in a nebulizer (GATC) for 1 minute, precipitated and resuspended in water.

The obtained nebulized genomic DNA is successively treated with Mung Bean Nuclease (Biolabs) (30 minutes at 30°C), T4 DNA polymerase (Biolabs) (10 minutes at 37°C) and Klenow enzyme (Pharmacia) (10 minutes at room temperature and 1 hour at 16°C).

DNA is then extracted, precipitated and resuspended in water.

1.A.2. Ligation of linkers to blunt-ended genomic DNA

Oligonucleotide PL160 (5' end phosphorylated) 1 μ g/ μ l and PL159 2μ g/ μ l.

Sequence of the oligo PL160: 5'-ATCCCGGACGAAGGCC-3'.

Sequence of the oligo PL159: 5'-GGCCTTCGTCCGG-3'.

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Linkers were preincubated (5 minutes at 95°C, 10 minutes at 68°C, 15 minutes at 42°C) then cooled down at room temperature and ligated with genomic DNA inserts at 4°C overnight.

Linkers were further removed on a separation column (Chromaspin TE 400, Clontech), according to the manufacturer protocol.

1.A.3. Vector preparation

pACTIIst is successively digest with BamHI restriction enzyme (Biolabs) for 1 hour at 37°C, dephosphorylated with Calf Intestine Phosphatase (CIP) (Biolabs) and filled in with dGTP using Vent DNA polymerase (exo-) (Biolabs), extracted, precipitated and resuspended in water.

1.A.4. Ligation between vector and insert of genomic DNA

The prepared vector is ligated overnight at 15°C with the genomic blunt ended DNA described in section 2 using T4 DNA ligase (Biolabs). The DNA is then precipitated and resuspended in water.

1.A.5. Library transformation in Escherichia coli

Transform DNA from section 1.A.4 into Electromax DH10B electrocompetent cells (Gibco BRL) with Cell Porator apparatus (Gibco BRL). Add 1 ml SOC medium and incubate transformed cells at 37°C for 1 hour. Add 9 ml volume of SOC medium per tube and plate on LB+ampicillin medium. Scrape colonies with liquid LB medium. Aliquot and freeze at -80°C.

The obtained collection of recombinant cell clones is named HGXBHP1 (CNCM No I-2181 deposited on April 13, 1999).

1.B. Collection transformation in Saccharomyces cerevisiae

The Saccharamyces cerevisiae strain (Y187 (MATα Gal4Δ Gal80Δ ade2-101 His3 Leu2-3, -112 Trp1-901 Ura3-52 URA3::UASGAL1-LacZ Met)) transformed with the HGXBHP1 H. pylori genomic DNA library.

The plasmid DNA contained in *E. coli* are extracted (Qiagen) from aliquoted *E. coli* frozen cells (1.A.5.).

Grow Saccharomyces cerevisiae yeast Y187 in YPGlu.

Yeast transformation is performed according to standard protocol (Giest et al. Yeast, 11, 355-360, 1995) using yeast carrier DNA (Clontech). This experiment leads to

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10⁴ to 5.10⁴ cells/μg DNA. Spread an estimating of 2.10⁴ transformanton DO-Leu (Drop-out) medium per plates. Aliquot and freeze at -80°C.

1.C. Construction of bait plasmid

The genomic amplification of the ORF is obtained by PCR using the Pfu proofreading Taq polymerase (Stratagene) and 200 ng of genomic DNA as template. PCR primers are chosen in regions flanking the ORF.

Set up the PCR program as followed:

Check amplification on agarose gel.

Purify PCR fragments with Qiaquick column (Qiagen) according to the manufacturer protocol.

Digest purified PCR fragments with adequate restriction enzymes.

Purify PCR fragments with Qiaquick column (Qiagen) according to the manufacturer protocol.

Ligate digested PCR fragments into an adequately digested and dephosphorylated bait vector (pAS2 $\Delta\Delta$) according to standard protocol (Maniatis et al.).

Transform into competent bacterial cells. Grow cells, extract DNA and sequence plasmid.

This protocole may also be applied to E. coli, S. aureus and S. pneumoniae genomic DNA.

<u>Example 2</u>: Screening the collection with the two-hybrid in yeast system

2.A. The mating protocol

We have chosen the mating two-hybrid in yeast system (firstly described by Fromont Racine et al., Nature Genetics, 1997, vol. 16, 277-282, Toward a functional analysis of the yeast genome through exhaustive two-hybrid screens) for its advantages but we could also screen the *Helicobacter pylori* collection in classical two-hybrid system as described in Fields *et al.* or in a yeast reverse two-hybrid system.

The mating procedure allows a direct selection on selective plates because the two fusion proteins are already produced in the parental cells. No replica plating is required.

This protocol is written for the use of the library transformed into the Y187 strain.

Before mating, transform S. cerevisiae (CG 1945 strain (MATa Gal4-542 Gal180-538 ade2-101 His3*200 Leu2-3,-112 Trp1-901 Ura3-52 Lys2-801 URA3::GAL4 17mers (X3)-CyC1TATA-LacZ LYS2::GAL1UAS-GAL1TATA-HIS3 CYH^R)) according to step 1.B. and spread on DO-Trp medium.

10 Day 1, morning: preculture

Preculture of Y187 cells carrying the bait plasmid obtained at step 1.C. in 20 ml DO-Trp medium. Grow at 30°C with vigorous agitation.

Day 1, late afternoon: culture

Measure OD_{600nm} of the DO-Trp preculture of Y187 cells carrying the bait plasmid preculture.

Inoculate 150 ml DO-Trp at OD600nm 0.006/ml, grow overnight at 30°C with vigorous agitation.

Day 2: mating

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medium and plates

20 5 YPGlu plates (Rich medium with glucose)

50 ml tube with 30 ml DO-Leu-Trp-His

100 ml flask with 20 ml of YPGlu

75 DO-Leu-Trp-His plates

2 DO-Leu plates

25 2 DO-Trp plates

2 DO-Leu-Trp plates

Measure OD_{600nm} of the DO-Trp culture. It should be around 1.

For the mating, you must use twice as many bait cells as library cells. To get a good mating efficiency, you must collect the cells at 10⁸ cells per cm².

Estimate the amount of bait culture (in ml) that makes up 80 OD600nm units for the mating with the prokaryote library.

Thaw a vial containing the HGXYHP1 library slowly on ice. Add the contents of the vial to 20 ml YPGlu. Let those cells recover at 30°C, under gentle agitation for 10 minutes.

Mating

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Put the 80 OD600nm units of bait culture into a 250 ml flask.

Add the HGXYHP1 library culture to the bait culture. Transfer the mixture of diploids into 50 ml sterile tubes. Centrifuge, discard the supernatant and resuspend in YPGlu medium.

Distribute cells on YPGlu Plates (Rich medium with glucose).

Incubate plates cells-up at 30°C for 4h30min.

Collection of mated cells

Wash and rinse plates and spread collected cells on DO-Leu-Trp-His plates.

Day 4

Selection of clones capable of growing on DO-Leu-Trp-His: this medium allows us to isolate diploid clones presenting an interaction.

Count the His+ colonies on control plates.

The number of His+ cell clones will define which protocol is to be processed : Upon 20.10^6 His+ colonies :

- if number of His+ cell clones > 285: then process overlay and then luminometry protocols on blue colonies (2.B and 2.C);
- if number of His+ cell clones < 285: process luminometry protocol (2.C).

The following step leads to the selection of the strongest interaction.

2.B. The X-Gal overlay assay

X-Gal overlay assay is performed directly on the selective medium plates after scoring the number of His⁺ colonies.

Material

Set up a waterbath. The water temperature should be 50°C.

- 0.5 M Na₂HPO₄ pH 7.5.
- 1.2 % Bacto-agar.
- 2 % X-Gal in DMF (dimethyl formamide).

- Overlay mixture: 0.25 M Na₂HPO₄ pH7.5, 0.5 % agar, 0.1 % SDS (Sodium dodecyl sulfate), 7 % DMF (LABOSI), 0.04 % X-Gal (ICN). For each plate, 10 ml overlay mixture are needed.
- DO-leu-trp-his plates.
- Sterile toothpicks.

Experiment

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Temperature of the overlay mix should be between 45 and 50°C.

Pour the overlay-mix over the plates in portions of 10 ml.

Collect them when the top layer is settled.

Incubate plates overlay-up at 30°C. Note the time.

Check for blue colonies regularly. If no blue colony appears, wait for overnight incubation. Mark with a pen and number the positives.

Streak the positives colonies on fresh DO-Leu-Trp-His plates with a sterile toothpick.

15 2.C. The luminometry assay

Grow His+ colonies overnight at 30°C in microtiter plates containing DO-Leu-Trp-His+Tetracyclin medium with shaking. The day after, dilute 15 times overnight culture into a new microtiter plate containing the same medium. Incubate 5 hours at 30°C with shaking. Dilute samples 5 times and read OD_{600nm}. Dilute again to obtain between 10 000 and 75 000 yeast cells/well in 100 µl final volume.

Per well, add 76 µl of One Step Yeast Lysis Buffer (Tropix), 20 µl SapphireII Enhancer (Tropix), 4 µl Galacton Star (Tropix), incubate 40 minutes at 30°C.

Measure the β -Gal read-out (L) using a Luminometer (Trilux, Wallach).

Calculate value of OD_{600mm}/L and select interacting preys having highest values.

At this step of the protocol, we have isolated diploid cell clones presenting interaction. The next step is now to identify polypeptides involved in the selected interactions.

Example 3: Identification of positive clones

30 3.A. PCR on yeast colonies

Introduction

PCR amplification of fragments of plasmid DNA directly on yeast colonies is a quick and efficient procedure to identify sequences cloned into this plasmid. It is directly derived from a published protocol (Wang H. et al., Analytical Biochemestry, 237, 145-146, 1996). However, it is not a standardized protocol: in our hands it varies from strain to strain, it is dependent of experimental conditions (number of cells, Taq polymerase source, etc). This protocol should be optimized to specific local conditions.

Materials

- For 1 well, PCR mix composition is:

 $32.5 \mu l$ water,

5 μl 10X PCR buffer (Pharmacia),

1 µl dNTP (10 mM each)

- 0.5 µl Taq polymerase (5u/µl) (Pharmacia),
- 0.5 µl oligonucleotide ABS1 10 pmole/µl: 5'-GCGTTTGGAATCACTACAGG-3',
- 0.5 μl oligonucleotide ABS2 10 pmole/μl: 5'-CACGATGCACGTTGAAGTG-3'.

- 1 N NaOH.

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Experiment

Grow positive colonies overnight at 30°C on a 96 well cell culture cluster (Costar), containing 150 μ l DO-Leu-Trp-His+Tetracyclin with shaking. Resuspend culture and transfer immediately 100 μ l on a Thermowell 96 (Costar).

Centrifuge 5 minutes at 4000 rpm at room temperature.

Remove supernatant.

Place the Thermowell in the thermocycler (GeneAmp 9700, Perkin Elmer) 5 minutes at 99.9°C and then 10 minutes at 4°C.

Add lysis buffer and incubate.

Centrifuge, transfer aliquot of supernatant in each well, add PCR mix, shake well.

Set up the PCR program as followed:

	94°C	3 minutes	
30	94°C	30 secondes	
	53°C	1 minute 30 secondes	x 35 cycles
	72°C	3 minutes	

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72°C 5 minutes

15°C °

Check the quality, the quantity and the length of the PCR fragment on agarose gel.

The length of the cloned fragment is the estimated length of the PCR fragment minus 300 base pairs that correspond to the amplified flanking plasmid sequences.

3.B. Plasmids rescue from yeast by electroporation

Introduction

The previous protocol of PCR on yeast cell may not be successful, in such a case, we rescue plasmids from yeast by electroporation. This experiment allows the recovery of prey plasmids from yeast cells by transformation of *E. coli* with a yeast cellular extract. We can then amplify the prey plasmid and sequence the cloned fragment.

Material

15 Plasmid rescue

Glass beads 425-600 µm (Sigma)

Phenol/chloroform (1/1) premixed with isoamyl alcohol (Amresco)

Extraction buffer: 2 % Triton X100, 1 % SDS, 100 mM NaCl, 10 mM TrisHCl pH 8.0, 1 mM EDTA pH 8.0.

Mix ethanol/NH₄Ac: 6 volumes ethanol with 7.5 M NH₄ Acetate, 70 % Ethanol and yeast cells in patches on plates.

Electroporation

SOC medium

M9 medium

Selective plates: M9-Leu+Ampicillin

2 mm electroporation cuvettes (Eurogentech)

Experiment

Plasmid rescue

Prepare cell patch on DO-Leu-Trp-His with cell culture of section 2.C.

Scrape the cell of each patch in Eppendorf tube, add 300 μ l of glass beads in each tube, then, add 200 μ l extraction buffer and add 200 μ l phenol:chloroform:isoamyl alcohol (25:24:1).

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Centrifuge tubes 10 minutes at 15000 rpm.

Transfer 180 µl supernatant to a sterile Eppendorf tube and add to each 500 µl ethanol/NH4Ac, vortex.

Centrifuge tubes 15 minutes, 15000 rpm at 4°C.

Wash pellet with 200 μ l 70 % ethanol, remove ethanol and dry pellet.

Resuspend pellet in 10 µl water. Store extracts at -20°C.

Electroporation

Material: Electrocompetent MC1066 cells prepared according to standard protocols (Maniatis).

10 Add 1 µl of yeast plasmid DNA-extract to pre-chilled Eppendorf tube, and keep on ice.

Mix 1 μ l plasmid yeast DNA-extract sample, add 20 μ l electrocompetent cells and transfer in a cold electroporation cuvette.

Set the Biorad electroporator on 200 ohms resistance, 25 μF capacity; 2.5 kVolts.

Place cuvette in the cuvette holder and electroporate.

Add 1 ml SOC into the cuvette and transfer the cell-mix into sterile Eppendorf tube.

Let cells recover for 30 minutes at 37°C, spin the cells down 1 minute, 4000x g and pour off supernatant. Keep about 100 µl medium and use it to resuspend the cells and spread them on selective plates (e.g. M9-Leu plates).

Incubate plates for 36 hours at 37°C.

Grow one colony and extract plasmids. Check presence and size of insert through enzymatic digestion and agarose gel. Sequence insert.

Example 4: Protein-Protein Interactions

For the purpose of this example, we have chosen to study *Helicobacter pylori's* protein-protein interactions.

For each bait, the previous protocol leads to the identification of prey polynucleotide sequences. In order to identify a protein-protein interaction, we need to characterize the obtained prey polypeptide sequence regarding the *Helicobacter pylori* genome.

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This may be accomplish with a software program names blastwun (available on the Internet site of the University of Washington : http://bioweb.pasteur.fr/seqanal/interfaces/blastwu.html, this is a development version of software for gene and protein identification through similarity searches of protein and nucleotide sequence databases).

Blastwun program compares prey polypeptide insert sequence (rescued from prey plasmid) with whole *Helicobacter pylori* genome (available on N.C.B.I. web site: http://www.ncbi.nlm.nih.gov under GenBank accession number AE000511). This comparison leads to prey polynucleotide localizations in *H. pylori* genome, each localization having a score depending on the homology of sequence. For each prey polynucleotide, we consider the localization with the highest score and, if the insert sequence is included in and is in phase with an Open Reading Frame, we can identify one prey polypeptide interacting with one bait polypeptide.

Helicobacter pylori ORF's sequences are available on the World-Wide Web site of The Institute for Genomic Research (TIGR) at http://www.tigr.org/tdb/mbd/hpdb/hpdb.html.

This web page allows several request concerning Helicobacter pylori's genome, in particular, its ORF sequence. To get the sequences of a specific ORF, click on the window named «HP#» and click search. This operation leads to a new web page presenting nucleic and peptide sequence of the specific ORF.

Table I: protein interaction in Helicobacter pylori (see hereafter)

Example 5: Identification of SID®

Experiment results in step 4. sequences of each prey fragment encoding for an interacting prey polypeptide.

By comparing and selecting the intersection of every isolated fragments that are included in the same polypeptide, we define the Selected Interacting Domain (SID®) see figure 7.

30 See results in Tables Π and III.

<u>Table I</u>: Interaction involving polypeptides including *Helicobacter pylori* ORF

Bait polypeptides	Interacting ORF
(ORF reference according to Tomb et al.)	(ORF reference according to Tomb et al.)
HP0047	HP0047
HP0047	HP0048
HP0047	HP0695
HP0061	HP0066
HP0061	HP0978
HP0061	HP1409
HP0064	HP0063
HP0066	HP0066
HP0067	HP0069
HP0067	HP0609
HP0067	НР0768
HP0067	HP0770
HP0067	HP0956
HP0068	HP0070
HP0068	HP0118
HP0069	HP0067
HP0070	HP0068
HP0070	HP0070
HP0071	HP0278
HP0071	HP0417
HP0071	HP0570
HP0071	HP0775
HP0071	HP1340
HP0071	HP1409
HP0072	HP1489
HP0073	HP0073
HP0073	HP0232

HP0073	HP0259
HP0073	HP0067
HP0073	HP0232
HP0073	HP0705
HP0268	HP1198
HP0289	HP0289
HP0289	HP0289
HP0289	HP0887
HP0289	HP0922
HP0289	HP1038
HP0289	HP1543
HP0289	HP0289
HP0289	HP0289
HP0289	HP0610
HP0289	HP1355
HP0311	HP0312
HP0338	HP0132
HP0338	HP0337
HP0391	HP0099
HP0391	HP0392
HP0691	HP0692
HP0691	HP1362
HP0697	HP0012
HP0697	HP0048
HP0697	HP0558
HP0697	HP0599
HP0697	HP0696
HP0697	HP0864
HP0697	HP1037
HP0697	HP1038
HP0697	HP1299

HP0697	HP1576
HP0776	HP0067
HP0776	HP0278
HP0776	HP1378
HP0776	HP1409
HP0797	HP0289
HP0797	HP0887
HP0797	HP1349
HP0797	HP1377
HP0797	HP1409
HP0800	HP0433
HP0800	HP0687
HP0800	HP0800
HP0800	HP0801
HP0800	HP0924
HP0800	HP1267
HP0800	HP1460
HP0801	HP0152
HP0801	HP0800
HP0801	HP1513
HP0868	HP0088
HP0868	HP0327
HP0868	HP0869
HP0868	HP1142
HP0874	HP0875
HP0875	HP0874
HP0887	HP0459
HP0887	HP0610
HP0887	HP0699
HP0887	HP0887
HP0887	HP1157

HP1460
HP1464
HP0610
HP0887
HP1157
HP1464
HP0072
HP0528
HP0657
HP0979
HP1583
HP0643
HP0818
HP1122
HP1198
HP1316
HP0392
HP0088
HP0268
HP0293
HP0452
HP0705
HP0775
HP0965
HP1032
HP1114
HP1124
HP1198
HP1274
HP1378
HP1411

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HP1198	HP1541
HP1198	HP1032
HP1198	HP1218
HP1230	HP1230
HP1230	HP1529
HP1231	HP1247
HP1244	HP0857
HP1244	HP1246
HP1246	HP0121
HP1246	HP0326
HP1246	HP0407
	HP0886
HP1246	
HP1246	HP1035
HP1246	HP1244
HP1246	HP1460
HP1247	HP1231
HP1247	HP1353
HP1293	HP1198

^{*} Tomb et al., 1997, Nature, 388, 539-547

As indicated page 547 in the document Tomb et al., the annotated *H. pylori* genome sequence and gene family alignments are avalaible on the World-Wide Web site at http://www.tigr.org/tdb/mbd/hpdb/hpdb.html. For each ORF referenced HPXXXX, the detailed nucleic sequence, and amino acids sequence encoded by, can be obtained on the World-Wide Web site at http://www.tigr.org/tdb/mbd/hpdb/hpdb.html. by introducing said reference HPXXXX (see example 4).

Table II:

Bait polypeptides	SID®
(ORF reference according to Tomb et al.)	Amino Acid Sequence (SEQ ID N°)
HP0868	2
HP0868	4
HP0868	6
HP0868	8
HP0800	10
HP0800	12
HP0800	14
HP0800	16
HP0800	18
HP0800	20
HP0800	22
HP0801	24
HP0801	26
HP0801	28
HP0887	30
HP0887	32
HP0887	34
HP0887	36
HP0887	38
HP0887	40
HP0887	42
HP0289	44
HP0289	46
HP0289	48
HP0289	50
HP0289	52
HP0289	54

HP0289	56
HP0289	58
HP0289	60
HP0289	62
HP0068	64
HP0068	66
HP0047	68
HP0047	70
HP0047	72
HP0069	74
HP0066	76
HP0268	78
HP1293	80
HP0061	82
HP0061	84
HP0061	86
HP0064	88
HP1198	90
HP1198	92
HP1198	· 94
HP1198	96
HP1198	98
HP1198	100
HP1198	102
HP1198	104
HP1198	106
HP1198	108
HP1198	110
HP1198	112
HP1198	114
HP1198	116

	110
HP1198	118
HP1231	120
HP1032	122
HP1032	124
HP1032	. 126
HP1032	128
HP1032	130
HP1230	132
HP1230	134
HP1529	136
HP0978	138
HP0978	140
HP0071	142
HP0071	144
HP0071	146
HP0071	148
HP0071	150
HP0071	152
HP0073	154
HP0073	156
HP0073	158
HP0935	160
HP0935	162 · ·
HP0935	164
HP0338	166
HP0338	168
HP1246	170
HP1246	172
HP1246	174
HP1246	176
HP1246	178

HP1246	180
HP1246	182
HP0797	184
HP0797	186
HP0797	188
HP0797	190
HP0797	192
HP0311	194
HP0067	196
HP0067	198
HP0067	200
HP0067	202
HP0067	204
HP1244	206
HP1244	208
HP1067	210
HP0875	212
HP0776	214
HP0776	216
HP0776	218
НР0776	220
HP0697	222
НР0697	224
НР0697	226
HP0697	228
HP0697	230
HP0697	232
HP0697	234
HP0697	236
HP0697.	238
HP0697	240
nrv09/	

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НР0887	242
HP0887	244
HP0887	246
HP0887	248
HP1247	250
HP1247	252
HP0874	254
HP0072	256
HP0391	258
HP0391	260
HP0070	262
HP0070	264
HP0691	266
HP0691	268
HP1198	270
	272
HP1198	274
HP0073	276
HP0073	
HP0073	278

Table III:

Bait polypeptides	SID ®
(ORF reference according to Tomb et al.)	Nucleic acid sequence (SEQ ID N°)
HP0868	1
HP0868	3
HP0868	5
HP0868	7
HP0800	9
, HP0800	11
HP0800	13
HP0800	15
HP0800	17
HP0800	19
HP0800	21
HP0801	23
HP0801	25
HP0801	27
HP0887	29
HP0887	31
HP0887	33
HP0887	35
HP0887	37
HP0887	39
HP0887	41
HP0289	43
HP0289	45
HP0289	47
HP0289	49
HP0289	51
HP0289	53

	55
HP0289	
HP0289	57
HP0289	59
HP0289	61
HP0068	63
HP0068	65
HP0047	67
HP0047	69
HP0047	71
HP0069	73
HP0066	75
HP0268	77
HP1293	79
HP0061	81
HP0061	83
HP0061	85
HP0064	87
HP1198	89
HP1198	91
HP1198	93
HP1198	95
HP1198	97
HP1198	99
HP1198	101
HP1198	103
HP1198	105
HP1198	107
HP1198	109
HP1198	111
HP1198	113
HP1198	115
	<u> </u>

HP1198	117
HP1231	119
HP1032	121
HP1032	123
HP1032	125
HP1032	127
HP1032	129
HP1230	131
HP1230	133
HP1529	135
HP0978	137
HP0978	139
HP0071	141
HP0071	143
HP0071	145
HP0071	147
HP0071	. 149
HP0071	151
HP0073	153
HP0073	155
HP0073	157
HP0935	159
HP0935	161
HP0935	163
HP0338	165
HP0338	167
HP1246	169
HP1246	171
HP1246	173
HP1246	175
HP1246	177

HP1246	179
HP1246	181
HP0797	183
HP0797	185
HP0797	187
HP0797	189
HP0797	191
	193
HP0311	
HP0067	195
HP0067	197
HP0067	199
HP0067	201
HP0067	203
HP1244	205
HP1244	207
HP1067	209
HP0875	211
HP0776	213
HP0776	215
HP0776	217
HP0776	219
HP0697	221
HP0697	223
HP0697	225
HP0697	227
HP0697	229
HP0697	231
HP0697	233
HP0697	235
HP0697	237
HP0697	239
111 0057	

HP0887	241
HP0887	243
HP0887	245
HP0887	247
HP1247	249
HP1247	251
HP0874	253
HP0072	255
HP0391	257
HP0391	259
HP0070	261
HP0070	263
HP0691	265
HP0691	267
HP1198	269
HP1198	271
HP0073	273
HP0073	275
HP0073	277
111 0013	

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Claims

- 1. A method for producing a collection of recombinant cell clones usable for two-hybrid systems comprising the steps of:
- 5 a) fragmenting DNA;
 - b) inserting polynucleotidic fragments obtained in step a) in plasmids in such a way that the expression of said plasmids in host cell leads to an hybrid polypeptide containing a specific domain capable of activating a reporter gene when associated with a complementary domain;
- 10 c) transforming cell clones with plasmids obtained in step b); and
 - d) optionally, selecting the transformed recombinant cell clones obtained in step c); wherein DNA of step a) is genomic DNA obtained from a prokaryotic micro-organism.
 - 2. A method according to claim 1, wherein the step a) of fragmenting DNA is carried by a nebulization process.
- 3. A method according to claim 1 or 2, wherein the prokaryotic microorganism is *Helicobacter pylori*.
 - 4. A method according claim 1 or 2, wherein the prokaryotic microorganism is Staphylococcus aureus.
 - 5. A method according claim 1 or 2, wherein the prokaryotic micro-organism is Streptococcus pneumoniae.
 - 6. A method according claim 1 or 2, wherein the prokaryotic micro-organism is Escherichia coli.
 - 7. Collection of recombinant cell clones usable for two-hybrid systems obtainable by a method according to anyone of claims 1 to 6.
 - 8. Collection of recombinant cell clones usable for two-hybrid systems, each recombinant cell clone containing a polynucleotide inserted in a plasmid whose expression leads to hybrid polypeptide containing a specific domain, wherein the said polynucleotide is a genomic DNA fragment obtained from a prokaryotic microorganism.
- 9. Collection of recombinant cell clones usable for two-hybrid systems according to claim 8 wherein said genomic DNA fragment is obtained by a fragmentation process by nebulization.

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- 10. Collection of recombinant cell clones according to anyone of claims 7 to 9, wherein the prokaryotic micro-organism is *Helicobacter pylori*.
- 11. Collection of recombinant cell clones according to anyone of claims 7 to 9, wherein the prokaryotic micro-organism is Staphylococcus aureus.
- 12. Collection of recombinant cell clones according to anyone of claims 7 to 9, wherein the prokaryotic micro-organism is Streptococcus pneumoniae.
- 13. Collection of recombinant cell clones according to anyone of claims 7 to 9, wherein the prokaryotic micro-organism is *Escherichia coli*.
- 14. Collection of recombinant cell clones according to anyone of claims 7 to 13, wherein the recombinant cell clones are selected from the group consisting of Gram+ or Gram- bacteria, yeasts, fungi and mammalian cells.
 - 15. Collection of recombinant cell clones according to claim 14, wherein the recombinant cell clones are selected from the group consisting of *Escherichia coli* bacteria and *Saccharomyces cerevisiae* yeast.
 - 16. Collection of recombinant cell clones according to claim 15, wherein the recombinant cell clones are *E. coli* bacteria.
 - 17. Collection of recombinant cell clones according to anyone of claims 7 to 16, wherein the plasmids comprise at least a nucleic sequence coding a promoter, a specific domain, a multicloning site where the said polypeptide is cloned, and a selection marker.
 - 18. Collection of recombinant cell clones according to anyone of claims 7 to 17, wherein the polynucleotide is inserted in the plasmid pACTIIst or pP6.
 - 19. Collection of recombinant cell clones according to claim 18, wherein the collection contains 10⁶ to 10⁷ recombinant *Escherichia coli* clones and wherein the proportion of different cell clones with insert is at least 60 %.
 - 20. Collection of recombinant cell clones according to claim 18 or 19 filed with CNCM on April 13, 1999 under number I-2181.
 - 21. Collection of recombinant cell clones according to claim 18 or 19 filed with CNCM on March 23, 2000 under number I-2416.
 - 22. Collection of recombinant cell clones according to claim 18 or 19 filed with CNCM on March 23, 2000 under number I-2414.

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- 23. Collection of recombinant cell clones according to claim 18 or 19 filed with CNCM on March 23, 2000 under number I-2415.
- 24. Collection of recombinant cell clones according to claim 18 or 19 filed with CNCM on March 23, 2000 under number I-2417.
- 25. Collection of recombinant cell clones according to claim 18, wherein the collection contains 10⁵ to 1.5 x 10⁶ haploid recombinant Saccharomyces cerevisiae clones and wherein the proportion of different cell clones with insert is at least 60 %.
- 26. Collection of recombinant cell clones according to claim 18 or 25 filed with CNCM on April 13, 1999 under number I-2182.
- 27. Collection of recombinant cell clones according to claim 18 or 25 filed with CNCM on March 23, 2000 under number I-2420.
 - 28. Collection of recombinant cell clones according to claim 18 or 25 filed with CNCM on March 23, 2000 under number I-2419.
 - 29. Collection of recombinant cell clones according to claim 18 or 25 filed with CNCM on March 23, 2000 under number I-2418.
 - 30. Collection of recombinant cell clones according to anyone of claims 7 to
 17, wherein the polynucleotide is inserted in the plasmid pAS2ΔΔ.
 - 31. Collection of recombinant cell clones according to anyone of claims 7 to 17, wherein the polynucleotide is inserted in a plasmid selected from the group consisting of pT25, pKT25, pUT18 and pUT18C.
 - 32. Kit for screening protein-protein interaction comprising a collection of recombinant cell clones usable for two-hybrid systems according to anyone of claims 7 to 31.
- 33. A yeast two-hybrid system method for identifying a recombinant cell
 25 clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:
 - a) mating at least one first haploid recombinant cell clone of a collection of recombinant cell clones according to claim 25 or 26 transformed with a plasmid containing the prey polynucleotide to be assayed with a second haploid recombinant S. cerevisiae cell clone transformed with a plasmid containing a bait polynucleotide encoding said bait polypeptide;
 - b) cultivating diploid cell obtained in step a) on selective medium; and

- c) selecting recombinant cell clones capable of growing on selective medium.
- 34. A yeast two-hybrid system method for identifying a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:
- a) identifying a recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide according to claim 33; and
 - b) characterizing the prey polynucleotide contained in each recombinant cell clone selected in step a).
- 35. A bacterial two-hybrid system method for identifying a recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:
 - a) transforming bacterial cell clones with a plasmid containing a bait polynucleotide encoding said bait polypeptide;
- b) rescuing prey plasmids containing prey polynucleotides from the collection according to claims 7 to 31;
 - c) transforming the recombinant bacterial cell clones obtained in step a) with the plasmid rescued in step b);
 - d) cultivating bacterial recombinant cells obtained in step c) on selective medium;
- 20 e) selecting recombinant cell clones capable of growing on selective medium.
 - 36. A bacterial two-hybrid system method for identifying a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:
 - a) identifying a bacterial recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide according to claim 35; and
 - b) characterizing the prey polynucleotide contained in each recombinant cell clone selected in step a).
- 37. Method according to anyone of claims 33 to 36, wherein the bait polypeptide is a human polypeptide.
 - 38. Method according to anyone of claims 33 to 36, wherein the bait polypeptide is a *Helicobacter pylori* polypeptide.

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- 39. Method according to anyone of claims 33 to 36, wherein the bait polypeptide is a Staphylococcus aureus polypeptide.
- 40. Method according to anyone of claims 33 to 36, wherein the bait polypeptide is a Streptococcus pneumoniae polypeptide.
- 41. Method according to anyone of claims 33 to 36, wherein the bait polypeptide is a *Escherichia coli* polypeptide.
- 42. A recombinant diploid yeast cell obtained by step a) of the method according to claim 33.
- 43. A recombinant diploid yeast cell obtained by the method according to claim 33.
 - 44. A set of two purified or isolated polynucleotides consisting of a first polynucleotide, or fragment thereof, encoding a prey polypeptide capable of interacting with a bait polypeptide and a second polynucleotide, or a fragment thereof having at least 12 consecutive nucleotides, encoding said bait polypeptide wherein the prey polynucleotide is identified by a method according to anyone of claims 34 and 36.
 - 45. A set of two purified or isolated polypeptides encoded by the set of two polynucleotides according to claim 44.
 - 46. Protein-protein interaction wherein the two interacting proteins consist of a set of two polypeptides according to claim 45.
 - 47. Protein-protein interaction according to claim 46, wherein the set of two polypeptides consists of two *Helicobacter pylori* polypeptides.
 - 48. Protein-protein interaction according to claim 46, wherein the set of two polypeptides consists of two *Staphylococcus aureus* polypeptides.
 - 49. Protein-protein interaction according to claim 46, wherein the set of two polypeptides consists of two Streptococcus pneumoniae polypeptides.
 - 50. Protein-protein interaction according to claim 46, wherein the set of two polypeptides consists of two Escherichia coli polypeptides.
 - 51. Isolated complex comprising at least the two polypeptides encoded by the set of two polynucleotides according to claim 44.
- 52. Isolated complex according to claim 51, characterized in that said complex comprises at least a polypeptide encoded by the ORF HP1198 and a polypeptide encoded by the ORF HP1293.

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- 53. Isolated complex according to claim 51, characterized in that said complex comprises at least a polypeptide encoded by the ORF HP1198 and a polypeptide encoded by the ORF HP0088.
- 54. Isolated complex according to claim 51, characterized in that said complex comprises at least a polypeptide encoded by the ORF HP1198 and a polypeptide encoded by the ORF HP1032.
- 55. A computable readable medium having stored thereon protein-protein interactions according to claim 46 to 50.
- 56. A computable readable medium according to claim 55, wherein the protein-protein interactions stored thereon is stored in a form of a map.
 - 57. A computable readable medium according to claim 55 or 56, wherein the protein-protein interactions stored thereon are linked to annotated database through Internet.
 - 58. A method for identifying a polynucleotide encoding a selecting interacting domain (SID®) of a prey polypeptide of interest from a prokaryotic microorganism capable of interacting with a bait polypeptide comprising the steps of:
 - a) selecting from prey polynucleotides identifyied by a method according to claim 34 or 36 all prey polynucleotides encoding a polypeptide capable of interacting with said bait polypeptide and containing a nucleic acid fragment identical to a nucleic fragment of the polynucleotide encoding the prey polypeptide of interest;
 - b) determining the polynucleotide common to said all prey polynucleotides selected in step a); and
 - c) identifying the polynucleotide determining in step b) as being the polynucleotide encoding the selected interacting domain (SID®) of said prey polypeptide of interest.
 - 59. Purified or isolated polynucleotide encoding a selecting interacting domain (SID®) of a prey polypeptide of interest from a prokaryotic micro-organism capable of interacting with a bait polypeptide obtainable by a method according to claim 58.
- 60. Purified or isolated polynucleotide according to claim 59 selected from the group consisting of:
 - a) a polynucleotide encoding an amino acids sequence identified by the reference indicated in the right column "SID®" in table II;

- b) a polynucleotide having the sequence identified by the reference indicated in the right column "SID®" in table III;
- c) fragment having at least 12 consecutive nucleotides of polynucleotide of a) or b), complement thereof, and RNA corresponding to said polynucleotide; and
- d) a polynucleotide having at least 80 % identity degree after alignment to a nucleic acid sequence of a polynucleotide of a) or b).
 - 61. Purified or isolated polypeptide selected from the group consisting of:
 - a) a polypeptide having an amino acids sequence identified by the reference indicated in the right column "SID®" in table II, and fragment thereof having at least 5 consecutive amino acids; and
 - b) a polypeptide encoded by a polynucleotide according to claim 59 or 60.
 - 62. Use of a polynucleotide according to claim 60 as a primer for amplification.
 - 63. Use of a polynucleotide according to claim 60 as a specific probe for detection.
 - 64. Cloning or expression vector containing a polynucleotide according to anyone of claims 59 and 60.
 - 65. Vector according to claim 64, wherein the vector is the plasmid pACTIIst, pAS2 $\Delta\Delta$ or pP6.
- 20 66. Vector according to claim 64, wherein the vector is the plasmid selected from the group consisting of pT25, pKT25, pUT18 and pUT18C.
 - 67. Vector according to claim 64, wherein the vector is self replicated.
 - 68. Vector according to claim 64 or 67, wherein the vector is a viral vector.
- 69. Vector according to claim 68, wherein the vector is chosen between an adenovirus, AAV, a retrovirus, a proxivirus or an herpes virus.
 - 70. Vector according to anyone of claims 64 to 69 including elements allowing expression and/or secretion of said polynucleotide in a host cell.
 - 71. Host cell transformed with a vector according to anyone of claims 64 to 70.
- Host cell according to claim 71, wherein the host cell is a prokaryotic cell.

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- 73. Host cell according to claim 71, wherein the host cell is an eukaryotic cell.
- 74. Method for producing a polypeptide according to anyone of claims 45 and 61, comprising the steps of:
- a) cultivating a host cell according to anyone of claims 71 to 73 under conditions and in culture medium allowing the growth of said host cell and the expression of said polypeptide; and
 - b) recovering said polypeptide directly from the culture medium or from said cultivated cell obtained in step a).
 - 75. Purified or isolated polypeptide obtained by the method according to claim 74.
 - 76. A method for selecting an agent capable of modulating the proteinprotein interaction of a step of two polypeptides according to claim 45 comprising the steps of:
- a) cultivating a recombinant cell clone containing a reporter gene expression of which is toxic for said recombinant cell clone and transformed with two plasmids wherein:
 - i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and a DNA binding domain;
- 20 ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and an activating domain capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting;
 - on a selective medium containing the agent to be tested and allowing the growth of said recombinant cell clone when the toxic reporter gene is not activated; and
 - b) selecting agent which is capable of inhibiting the growth of the recombinant cell clone cultivated in step a).
 - 77. A method for selecting an agent capable of modulating the proteinprotein interaction of a set of two polypeptides according to claim 45 comprising the steps of:

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- a) cultivating a permeable recombinant cell clone containing a reporter gene expression of which is toxic for said recombinant cell clone and transformed with two plasmids wherein:
 - i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and the first domain of an enzyme;
 - ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and the second part of said enzyme capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting, said interaction restoring the activity of the enzyme;

on a selective medium containing the agent to be tested and allowing the growth of said recombinant cell clone when the toxic reporter gene is not activated; and

- b) selecting agent which is capable of inhibiting the growth of the recombinant cell clone cultivated in step a).
- 78. A method according to claim 77, for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198, or a fragment or homologuous polypeptide thereof, and a polypeptide encoded by the ORF HP1293, or a fragment or homologuous polypeptide thereof.
- 79. A method according to claim 77, for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198, or a fragment or homologuous polypeptide thereof, and a polypeptide encoded by the ORF HP0088, or a fragment thereof or homologuous polypeptide thereof.
- 80. A method according to claim 77, for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198, or a fragment or homologuous polypeptide thereof, and a polypeptide encoded by the ORF HP1032, or a fragment or homologuous polypeptide thereof.
 - 81. Modulator agent selected by the method according to claim 76 or 77.
- 82. Kit for screening a modulator agent comprising at least one recombinant transformed cell clone according to step a) of claim 76 or 77.
 - 83. Use of a polypeptide according to anyone of claims 45 and 61 for the modulation of *Helicobacter pylori*'s protein interaction.

- 84. Method for the production of monoclonal or polyclonal comprising the step of immunization of an animal or human organism with an immunogenic agent comprising a polypeptide according to anyone of claims 45 and 61, a vector according to anyone of claims 65 to 70 or a host cell according to anyone of claims 71 to 73.
 - 85. Antibody obtained by the method according to claim 84.
- 86. A pharmaceutical composition comprising a compound selected from the group consisting of:
- a) a polynucleotide according to anyone of claims 59 and 60;
- b) a polypeptide according to anyone of claims 45 and 61;
- 10 c) a vector according to anyone of claims 62 to 70;
 - d) a host cell according to anyone of claims 71 to 73;
 - e) a modulator agent according to claim 80; and
 - f) an antibody according to claim 85.
- 87. A pharmaceutical composition according to claim 86, wherein said composition is administered by any route such as intravenous route, intramuscular route, oral route, or mucosal route with an acceptable physiological carrier and/or adjuvant.

PCT/IB00/00603

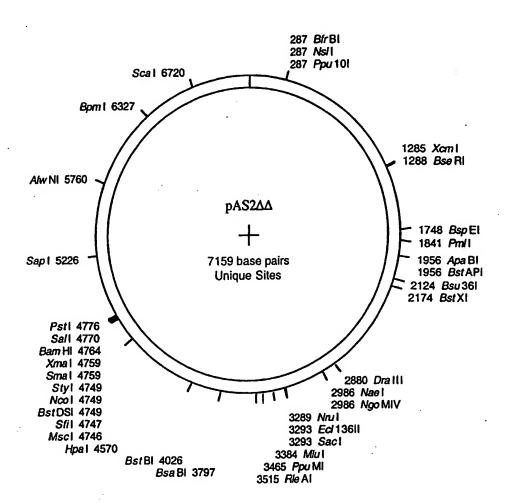


FIGURE 1

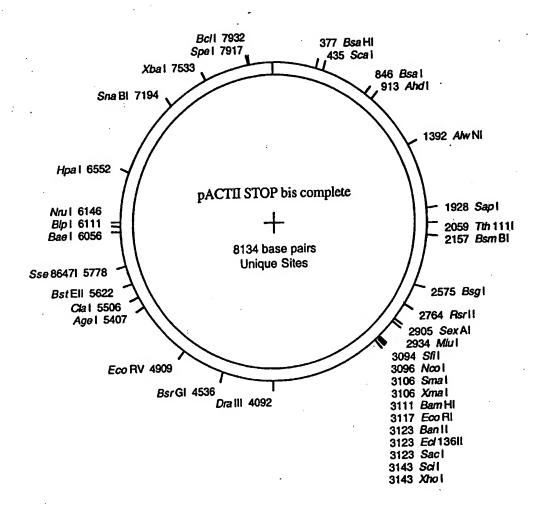
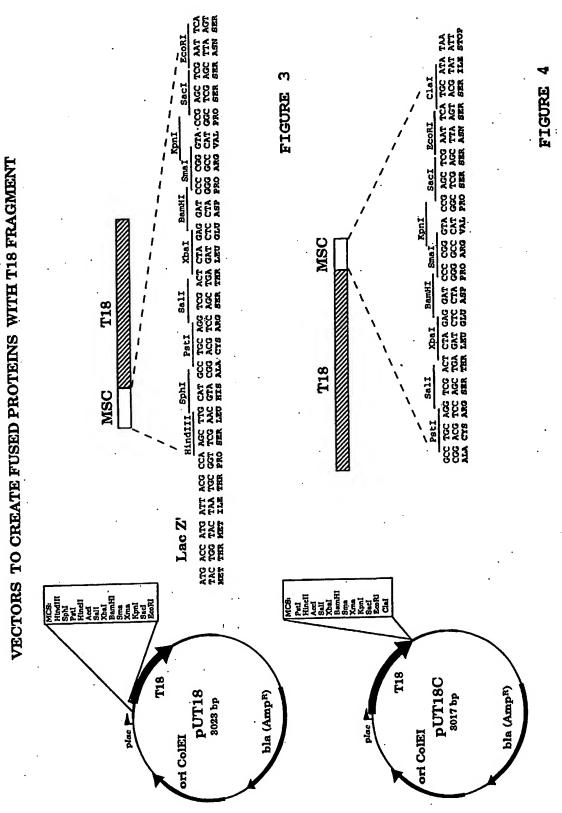
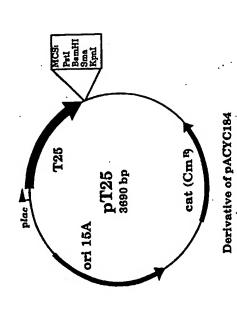


FIGURE 2

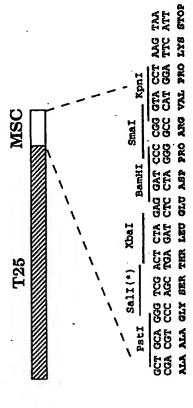


VECTORS TO CREATE FUSED PROTEINS WITH T25 FRAGMENT



(*) Restriction sites are not unique

FIGURE 5



MCS: Pst! BamHi Sma Kpal

T26

plac |

pKT25 342 bp

ori 15A

(*) Restriction site is not unique

Derivative of pSU40

kan (Km^R)

FIGURE 6

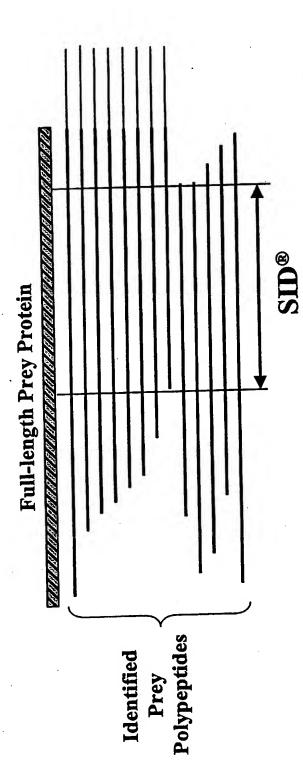


FIGURE 7

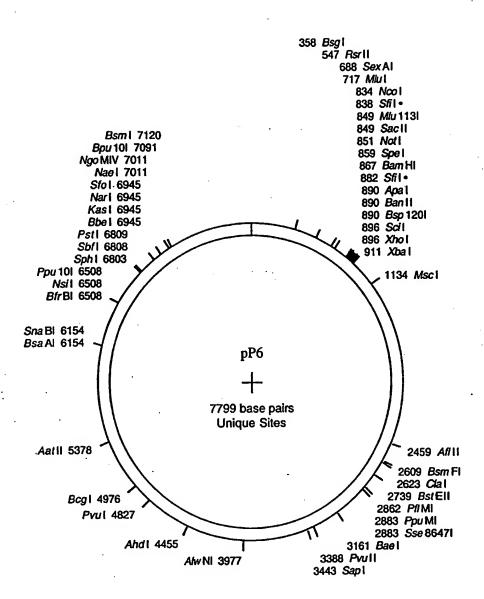


FIGURE 8

SEQUENCE LISTING

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<130> D18015
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<151> 1999-04-30
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                                                                    96
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                                  25
gtg act aaa gag cct atc agt ttg gaa acc cca gtc ggc aat gat gat
                                                                    144
Val Thr Lys Glu Pro Ile Ser Leu Glu Thr Pro Val Gly Asn Ásp Ásp
                              40
          35
gat ggc aag ttt ggg gat ttc gtg gaa gat aag aat atc gtc agc tcc
                                                                    192
Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Ile Val Ser Ser
                          55
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                                                                    240
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                                          75
                      70
 ttg gat cag ttg aat gag cga gaa aaa gcg gtg atc cgc atg cgt ttt
                                                                    288
 Leu Asp Gln Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Met Arg Phe
                                      90
                  85
 ggg ctt tta gac gat gaa agc gat cga act tta gaa gaa att ggc aag
                                                                    336
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                                 105
             100
 gaa ttg aat gtt act aga gaa agg gtg cgc cag att gaa agc tct gcg
                                                                    384
 Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser Ser Ala
                             120
 att aaa aaa ttg aga agc ccg cag tac ggg cgc att tta aga aac tat
                                                                     432
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Leu Asp Gln Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Met Arg Phe
                                      90
Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Ile Gly Lys
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                                 105
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Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser Ser Ala
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Val Gly Ser Ile Thr Lys Ile Asn Phe Phe His Lys His Gly Tyr Leu
                                  25
ggg att tat aaa aac cct ttt ttg aaa aat ggg gga gaa acg att tta
Gly Ile Tyr Lys Asn Pro Phe Leu Lys Asn Gly Gly Glu Thr Ile Leu
                             40
                                                  45
         35
aaa gcc ttg gaa ttt atc gct ttt gaa gag ttc caa tta cat tct ttg
                                                                   192
Lys Ala Leu Glu Phe Ile Ala Phe Glu Glu Phe Gln Leu His Ser Leu
                         55
cat tta gaa gtg atg gaa aac aat ttc aaa gcg atc gct ttt tat gaa
                                                                    240
His Leu Glu Val Met Glu Asn Asn Phe Lys Ala Ile Ala Phe Tyr Glu
                     70
aaa aac cat tat gag tta gag ggg cgt ttg aaa ggc ttt att tct aaa
                                                                    288
Lys Asn His Tyr Glu Leu Glu Gly Arg Leu Lys Gly Phe Ile Ser Lys
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Asp Lys Glu Phe Ile Asp Val Leu Leu Tyr Tyr Lys Asp Lys Lys Gly
                                 105
                                                     110
            100
                                                                    363
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                              40
Lys Ala Leu Glu Phe Ile Ala Phe Glu Glu Phe Gln Leu His Ser Leu
                                              60
                          55
His Leu Glu Val Met Glu Asn Asn Phe Lys Ala Ile Ala Phe Tyr Glu
```

```
70
 65
Lys Asn His Tyr Glu Leu Glu Gly Arg Leu Lys Gly Phe Ile Ser Lys
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                 85
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            100
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                                      10
att atc act caa ggc aat gaa atg cgt ttg ttg tct tta gaa atg tta
                                                                   96
Ile Ile Thr Gln Gly Asn Glu Met Arg Leu Leu Ser Leu Glu Met Leu
                                  25
                                                                   102
gcg gaa
Ala Glu
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Ala Glu
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                                      10
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                                                                    96
 Lys Ile Val Glu Thr Glu Gln Lys Asn Gln Gln Thr Lys Leu Asp Thr
              20
 gaa aat ttg aaa ata att att gaa act ttg aga agt aaa atc aat ggg
                                                                    144
 Glu Asn Leu Lys Ile Ile Ile Glu Thr Leu Arg Ser Lys Ile Asn Gly
 aat cag caa aag atg ctt gat aaa agt aaa gaa atg agc aga aat ttt
                                                                    192
 Asn Gln Gln Lys Met Leu Asp Lys Ser Lys Glu Met Ser Arg Asn Phe
                          · 55
 aag ott gat ago act aaa aac gag ata gac goa att aaa gat ttg att
                                                                    240
 Lys Leu Asp Ser Thr Lys Asn Glu Ile Asp Ala Ile Lys Asp Leu Ile
 aaa aag gct aat gag caa ata gcc aat tat aat gag atg ata aag gat
                                                                    288
 Lys Lys Ala Asn Glu Gln Ile Ala Asn Tyr Asn Glu Met Ile Lys Asp
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 att gaa aaa cag aaa aag agt tgt aag gaa caa act tgg aaa ttt cta
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```
Ile Glu Lys Gln Lys Lys Ser Cys Lys Glu Gln Thr Trp Lys Phe Leu
                                105
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gtc aat gaa ttt aaa agt gat ata caa gaa tat aat aaa aag tat tgc
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Val Asn Glu Phe Lys Ser Asp Ile Gln Glu Tyr Asn Lys Lys Tyr Cys
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                            120
        115
ggt ttg gag aaa gga ata aac aat tta gag aaa gca att agt gaa aat
                                                                   432
Gly Leu Glu Lys Gly Ile Asn Asn Leu Glu Lys Ala Ile Ser Glu Asn
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                                                                   462
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Asn Gln Gln Lys Met Leu Asp Lys Ser Lys Glu Met Ser Arg Asn Phe
                         55
Lys Leu Asp Ser Thr Lys Asn Glu Ile Asp Ala Ile Lys Asp Leu Ile
                     70
Lys Lys Ala Asn Glu Gln Ile Ala Asn Tyr Asn Glu Met Ile Lys Asp
                                     90
                 85
Ile Glu Lys Gln Lys Lys Ser Cys Lys Glu Gln Thr Trp Lys Phe Leu
                                105
                                                     110
Val Asn Glu Phe Lys Ser Asp Ile Gln Glu Tyr Asn Lys Lys Tyr Cys
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                                                125
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Leu Gln Val Leu Glu Cys Glu Asn Cys Ser Met Thr Tyr Tyr Asp Arg
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                                                      30
             20
gat tat aat aga gaa tgt gag att tgc cct tat tgc gat gct aaa aaa
Asp Tyr Asn Arg Glu Cys Glu Ile Cys Pro Tyr Cys Asp Ala Lys Lys
cet gte aga ett gta gea aca agt tat tae caa aag age gaa gtt ttt
                                                                   192
Pro Val Arg Leu Val Ala Thr Ser Tyr Tyr Gln Lys Ser Glu Val Phe
                                             60
                         55
tat ttt gtc tcg aat ttt aca gac cct att ttt tta ccg aca acc tta
                                                                   240
Tyr Phe Val Ser Asn Phe Thr Asp Pro Ile Phe Leu Pro Thr Thr Leu
                     70
                                         75
 65
ttt aag ggg att gaa gtg gtt aaa agc gaa tgg gag ttt gca gag att
                                                                   288
Phe Lys Gly Ile Glu Val Val Lys Ser Glu Trp Glu Phe Ala Glu Ile
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```
85
                                      90
                                                                   336
gct aat aat ata ttg att ttt cat cat gac ata caa caa gaa aag att
Ala Asn Asn Ile Leù Ile Phe His His Asp Ile Gln Gln Glu Lys Ile
                                105
ctc att aat aat aaa aga ttg gat cac tat agg ata gaa ata gat tta
                                                                   384
Leu Ile Asn Asn Lys Arg Leu Asp His Tyr Arg Ile Glu Ile Asp Leu
        115
                            120
gaa aaa gaa ttg act att tca tac aat ggt ttt tta att aag gtt caa
                                                                   432
Glu Lys Glu Leu Thr Ile Ser Tyr Asn Gly Phe Leu Ile Lys Val Gln
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Lys Cys
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Asp Tyr Asn Arg Glu Cys Glu Ile Cys Pro Tyr Cys Asp Ala Lys Lys
Pro Val Arg Leu Val Ala Thr Ser Tyr Tyr Gln Lys Ser Glu Val Phe
Tyr Phe Val Ser Asn Phe Thr Asp Pro Ile Phe Leu Pro Thr Thr Leu
Phe Lys Gly Ile Glu Val Val Lys Ser Glu Trp Glu Phe Ala Glu Ile
                                     90
Ala Asn Asn Ile Leu Ile Phe His His Asp Ile Gln Gln Glu Lys Ile
                                105
Leu Ile Asn Asn Lys Arg Leu Asp His Tyr Arg Ile Glu Ile Asp Leu
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Lys Cys
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                                                                   96
Thr Leu Phe Val Ile Gly Phe Met Ser Cys Ser Ala Arg Leu Pro Ile
                                 25
tat gtg ctg ttt gta ggc tcg ttt ttc cct tct tca agt gct ggg ttt
Tyr. Val Leu Phe Val Gly Ser Phe Phe Pro Ser Ser Ser Ala Gly Phe
gtg ctg ttt tgc att tat att ttg ggg gcg gtt gtg gcg tta gtg atg
                                                                   192
Val Leu Phe Cys Ile Tyr Ile Leu Gly Ala Val Val Ala Leu Val Met
gcc aaa tta ctc aaa tta agc gtg ttt aaa gga caa acc gaa tct ttt
                                                                   240
Ala Lys Leu Leu Lys Leu Ser Val Phe Lys Gly Gln Thr Glu Ser Phe
65
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	agt		+	00	222	tca	ctt	tct		ctt	aaa	aaq	gct	ggg	act	336
TTC	Ser	Tle	Tur	Thr	T.vs	Ser	Leu	Ser	Tyr	Leu	Lys	Lys	Ála	Gly	Thr	
			100					105					110			
tac	att	tta	~+~	gga	qcq	att	tta	atc	tgg	ttt	atg	tct	caa	tac	cct	384
Tur	Ile	Leu	Val	Glv	Ala	Ile	Leu	Ile	Trp	Phe	Met	Ser	Gln	Tyr	Pro	
		115					120					123				400
aaa	agc	gat	gcg	gcc	atg	aaa	gct	tat	aaa	caa	gaa	agc	ttg	tta	gtg	432
Lys	Ser	Asp	Ala	Ala	Met	Lys	Ala	Tyr	Lys	Gln	GIU	Ser	Leu	ren	val	•
	120			-		135					T40					480
aat	aag	gat	acc	act	ctt	tca	agc	gaa	gct	aaa	gaa	Clu	Tue	LLa	Lve	400
Asn	Lys	Asp	Thr	Thr	Leu	Ser	Ser	GIU	Ala	155	GIU	Ģīu	пуз	neu	160	
145					150			220	22 t		222	aat	aσc	att		528
gaa	tta Leu	aaa	aca	gaa	ttg	gat	Tue	Lvs	Asn	Leu	Lvs	Asn	Ser	Ile	Val	•
Glu	Leu	Lys	Thr		тėп	Asp	цуз	цуз	170		-,-	••••		175		
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gga	Arg	Glv	999 61 v	Δla	Tur	Leu	Glu	Lvs	Val	Phe	Ser	Pro	Met	Asp	Phe	
_			180					185					130			
gat	tgg	cat	++~	agt	ata	tcg	ctt	gta	acc	gga	ttt	atg	gct	aaa	gag	624
Asp	Trp	Ara	Leu	Ser	Val	Ser	Leu	Val	Thr	Gly	Phe	met	Ala	Lys	Glu	
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ata	gtg	gtt	tct	act	ttg	ggc	gtg	ttg	ttt	tct	tta	ggg	gat	caa	aat	672
Val	Val	Val	Ser	Thr	Leu	Gly	Val	Leu	Phe	Ser	ren	GIA	Asp	GIN	Asn	
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		Ser	Asp	Ala		Arg	GTA	116	neu	235	БУЗ	GIU	101		Val 240	
225			-4-	aat	230	ato	. ata	ÉÉÉ	ata		ttt	tat	ato	cct	tgt	768
cct	agc	gga	alc Tlo	Mla	Phe	Tle	Val	Phe	Val	Met	Phe	Tyr	Ile	Pro	Cys	
				245				•	250					255		
+++	aca	aca	acc	att	act	ttt	ggt	agg	gaa	gcg	gga	ggg	ata	aag	ttt	816
Phe	Ala	Ala	Thr	Ile	Thr	Phe	Gly	Arg	Glu	Ala	Gly	Gly	116	: Lys	Phe	
			260					265					2/0	,		064
gta	gcg	tat	tta	ttc	atc	ttc	aca	acc	gtt	gta	gcg	tat	gco	ו דננ	tcc	864
Val	Ala	Tyr	Leu	Phe	Ile	Phe	Thr	Thr	Val	Val	Ala	TAT	WIG	Pne	Ser	
		275	1				280			+		285	,			897
ttg	ata	gct	ttt	tat	gcg	act	caa	att	Ley	yıı Vəl						
Leu	Ile		Phe	Tyr	Ala	295	GIII	116	пеп	Val	•					
-00	290					293	,									
	.0> 1 .1> 2												•			
	2> P															
	3> H		obac	ter	pylo	ri										
- 40	10 1	2												_		
Ala	Tvr	Met	. Ala	Thr	Arg	Thr	Leu	Gln	Asn	Туг	Asn	Glu	Arg	J Let	Ile	
1	ì	•		5	•				10)				Τ-	,	
Thi	Leu	Phe	. Val	. Ile	Gly	Phe	Met	Ser	Cys	Ser	Ala	Arc	l rei	l PEC	Ile	
			20)				25					٦١	,		
Туз	c Val	. Lev	Phe	Val	. Gly	Ser	: Phe	Phe	Pro	Sei	Ser	45	: WIG	a GI	Phe	
		35	5		_		40	01		. 17-1	17-1			ı Val	Met	
Va]	L Leu	Ph∈	e Cys	ille	Tyr			GIY	ATO	l val	60	. Ale	, DC		Met	
	50)	_	•	. 7	55) . !!!	Dho	Tare	. G1s			r Gla	ı Sei	Phe	
	_	Lev	ı Let	ı r. As			. val	rne	n y s	75	, 511				Phe 80	
65	 .		. M-1	. 10	70	, Т.,	- D	Pha	Pro			Arc	y Met	t Val	l Tyr	
Ile	e Met	GIL	ı met	. PIC		, 1 Y J	. AL	,	90)	r			9	5	
D.		. Tle	<u>.</u> ጥ፡፡ ፣	o. Tht	, Ive	Ser	Len	. Ser			Lys	Ly	a Ala	a Gly	y Thr	
P.D.	e 261	. 110	100		,-			105	_		-	_	11	0		
				•												

```
Tyr Ile Leu Val Gly Ala Ile Leu Ile Trp Phe Met Ser Gln Tyr Pro
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Lys Ser Asp Ala Ala Met Lys Ala Tyr Lys Gln Glu Ser Leu Leu Val
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Asn Lys Asp Thr Thr Leu Ser Ser Glu Ala Lys Glu Glu Lys Leu Lys
                                        155
                    150
Glu Leu Lys Thr Glu Leu Asp Lys Lys Asn Leu Lys Asn Ser Ile Val
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Gly Arg Gly Gly Ala Tyr Leu Glu Lys Val Phe Ser Pro Met Asp Phe
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Asp Trp Arg Leu Ser Val Ser Leu Val Thr Gly Phe Met Ala Lys Glu
                            200
Val Val Val Ser Thr Leu Gly Val Leu Phe Ser Leu Gly Asp Gln Asn
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Glu Lys Ser Asp Ala Phe Arg Gly Ile Leu Arg Lys Glu Val Ser Val
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Pro Ser Gly Ile Ala Phe Ile Val Phe Val Met Phe Tyr Ile Pro Cys
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Phe Ala Ala Thr Ile Thr Phe Gly Arg Glu Ala Gly Gly Ile Lys Phe
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Glu Ala Cys Ala Lys Asn Phe Gly Ala Phe Cys Val Phe Val Gly Ile
                                 25
gtg aga aaa gag gat aac att caa ggc ttg agt ttt gat att tat gaa
                                                                   144
Val Arg Lys Glu Asp Asn Ile Gln Gly Leu Ser Phe Asp Ile Tyr Glu
                                                 45
                             40
         35
gcg cta tta aag act tgg ttt gaa aaa tgg cac cat aaa gcc aaa gat
                                                                   192
Ala Leu Leu Lys Thr Trp Phe Glu Lys Trp His His Lys Ala Lys Asp
                         55
ttg ggc gtg gtg tta aaa atg gcg cac agc ctg ggc gat gtt ttg ata
                                                                   240
Leu Gly Val Val Leu Lys Met Ala His Ser Leu Gly Asp Val Leu Ile
                                         75
                     70
gga caa agc tca ttt tta tgc gtt tca atg gga aag aat aga aaa aat
                                                                   288
Gly Gln Ser Ser Phe Leu Cys Val Ser Met Gly Lys Asn Arg Lys Asn
gcc tta gaa cta tac gaa aat ttt att gaa gat ttt aag cat aac gct
                                                                   336
Ala Leu Glu Leu Tyr Glu Asn Phe Ile Glu Asp Phe Lys His Asn Ala
                                105
cct att tgg aaa tac gat tta atc cat aat aaa cgc att tat gct aaa
                                                                   384
Pro Ile Trp Lys Tyr Asp Leu Ile His Asn Lys Arg Ile Tyr Ala Lys
                            120
gaa aga agc cac cct tta aaa ggg agc ggg ctt tta gct
                                                                   423
Glu Arg Ser His Pro Leu Lys Gly Ser Gly Leu Leu Ala
                        135
    130
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<211> 156

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<212> PRT
<213> Helicobacter pylori
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Ile Gln Gly Ala Leu Asp Thr Arg Glu Leu Leu Lys Ala Tyr Gln Glu
                                     10
Glu Ala Cys Ala Lys Asn Phe Gly Ala Phe Cys Val Phe Val Gly Ile
                                 25
Val Arg Lys Glu Asp Asn Ile Gln Gly Leu Ser Phe Asp Ile Tyr Glu
Ala Leu Leu Lys Thr Trp Phe Glu Lys Trp His His Lys Ala Lys Asp
                         55
Leu Gly Val Val Leu Lys Met Ala His Ser Leu Gly Asp Val Leu Ile
                                         75
Gly Gln Ser Ser Phe Leu Cys Val Ser Met Gly Lys Asn Arg Lys Asn
                                     90
                . 85
Ala Leu Glu Leu Tyr Glu Asn Phe Ile Glu Asp Phe Lys His Asn Ala
                                105
            100
Pro Ile Trp Lys Tyr Asp Leu Ile His Asn Lys Arg Ile Tyr Ala Lys
                                                125
                            120
       115
Glu Arg Ser His Pro Leu Lys Gly Ser Gly Leu Leu Ala
                        135
  130
<210> 15
<211> 216
<212> DNA
<213> Helicobacter pylori
<220>
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<222> (1)..(216)
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gta gaa gtg cga ttt ttt gga ccc ata aaa gaa gaa aat ttt ttc atc
Val Glu Val Arg Phe Phe Gly Pro Ile Lys Glu Glu Asn Phe Phe Ile
                                     10
aaa gcg aat gat ttg aag gaa tta aga gcg att tta caa gaa aaa gag
Lys Ala Asn Asp Leu Lys Glu Leu Arg Ala Ile Leu Gln Glu Lys Glu
                                  25
             20
ggc tta aaa gag tgg ttg ggc gtt tgc gcg ata gcc ctt aat gat cat
Gly Leu Lys Glu Trp Leu Gly Val Cys Ala Ile Ala Leu Asn Asp His
                             40
 tta ata gac aat tta aac acg cct tta aaa gat ggc gat gta ata agt
                                                                    192
 Leu Ile Asp Asn Leu Asn Thr Pro Leu Lys Asp Gly Asp Val Ile Ser
                         55
     50
                                                                    216
 ttg ttg cca ccg gtt tgt ggg ggc
 Leu Leu Pro Pro Val Cys Gly Gly
 65
 <210> 16
 <211> 72
 <212> PRT
 <213> Helicobacter pylori
 <400> 16
 Val Glu Val Arg Phe Phe Gly Pro Ile Lys Glu Glu Asn Phe Phe Ile
                                      10
 Lys Ala Asn Asp Leu Lys Glu Leu Arg Ala Ile Leu Gln Glu Lys Glu
              20
 Gly Leu Lys Glu Trp Leu Gly Val Cys Ala Ile Ala Leu Asn Asp His
                                                  45
                              40
 Leu Ile Asp Asn Leu Asn Thr Pro Leu Lys Asp Gly Asp Val Ile Ser
                          55
 Leu Leu Pro Pro Val Cys Gly Gly
 <210> 17
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<212> DNA
<213> Helicobacter pylori
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<221> CDS
<222> (1)..(156)
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aac gag caa aaa cag caa ttg att gaa ggg gtt tca gat ttg atg gtt
                                                                   48
Asn Glu Gln Lys Gln Gln Leu Ile Glu Gly Val Ser Asp Leu Met Val
aag gtg ctg aat aaa aat aag gct tct att gtg gtc att ata gat gag
                                                                    96
Lys Val Leu Asn Lys Asn Lys Ala Ser Ile Val Val Ile Ile Asp Glu
                                  25
             20
gtc gat tct aat aat tat ggt ctt ggg ggc gag agc gtc cat cat ttg
                                                                    144
Val Asp Ser Asn Asn Tyr Gly Leu Gly Gly Glu Ser Val His His Leu
                              40
         35
                                                                    156
agg caa aaa aac
Arg Gln Lys Asn
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<212> PRT
<213> Helicobacter pylori
Asn Glu Gln Lys Gln Gln Leu Ile Glu Gly Val Ser Asp Leu Met Val
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                                      10
  1
Lys Val Leu Asn Lys Asn Lys Ala Ser Ile Val Val Ile Ile Asp Glu
                                                      30
                                  25
             20
Val Asp Ser Asn Asn Tyr Gly Leu Gly Gly Glu Ser Val His His Leu
                              40
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Arg Gln Lys Asn
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 Ile Tyr Ala Pro Ile Leu Ala Gly Leu Ala Ser Asn Asn Lys Tyr Ser
                                      10
   1
 tta att ggc tcc gca aga gcg acg atc caa ctg ctc agc ttt gaa gtg
                                                                    96
 Leu Ile Gly Ser Ala Arg Ala Thr Ile Gln Leu Leu Ser Phe Glu Val
                                  25
 gte age act tta ace att eta gee eec tta atg gtg gta gga teg ete
 Val Ser Thr Leu Thr Ile Leu Ala Pro Leu Met Val Val Gly Ser Leu
                                                   45
                              40
          35
 tot tta gtg gaa atc aat cat tac caa agc ggt ggg ttt tta gac tgg
                                                                     192
 Ser Leu Val Glu Ile Asn His Tyr Gln Ser Gly Gly Phe Leu Asp Trp
                                               60
                          55
 ctt gtg ttt aag cag cct cta gcg ttt gtt ttg ttt ttg atc gca agt
                                                                     240
 Leu Val Phe Lys Gln Pro Leu Ala Phe Val Leu Phe Leu Ile Ala Ser
                      70
  65
 tat gcc gaa ttg aat cga acc ccc ttt gac ttg cta gag cat gaa gcc
                                                                     288
 Tyr Ala Glu Leu Asn Arg Thr Pro Phe Asp Leu Leu Glu His Glu Ala
                                       90
                  85
 gag atc gtg gcg ggg tat tgc acc gaa tac agc ggc ttg aaa tgg ggc
                                                                     336
 Glu Ile Val Ala Gly Tyr Cys Thr Glu Tyr Ser Gly Leu Lys Trp Gly
                                                      110
                                 105
 atg ttc ttt tta gcg gaa tac gcg cat tta ttc gct ttt tct ttt gtg
                                                                     384
```

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Met Phe Phe Leu Ala Glu Tyr Ala His Leu Phe Ala Phe Ser Phe Val
                            120
att tot att gtg ttt ttt ggc ggg ttt aac gca tgg ggc ttt atc cct
Ile Ser Ile Val Phe Phe Gly Gly Phe Asn Ala Trp Gly Phe Ile Pro
                                            140
                        135
gga ggc ata gcg att ttg att aaa gcg ggc ttt ttt gtc ttt tta tcc
Gly Gly Ile Ala Ile Leu Ile Lys Ala Gly Phe Phe Val Phe Leu Ser
                                        155
                    150
atg tgg gtt aga gcg act tat ccg cat gtg cgc cca gac caa ctg atg
                                                                   528
Met Trp Val Arg Ala Thr Tyr Pro His Val Arg Pro Asp Gln Leu Met
                                    170
                165
gat atg tgc tgg aaa atc atg ctg cct tta gcg tta ttg aac att gtg
Asp Met Cys Trp Lys Ile Met Leu Pro Leu Ala Leu Leu Asn Ile Val
                                185
            180.
cta acg ggc att atc att tta att
                                                                   600
Leu Thr Gly Ile Ile Ile Leu Ile
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<213> Helicobacter pylori
Ile Tyr Ala Pro Ile Leu Ala Gly Leu Ala Ser Asn Asn Lys Tyr Ser
                                     10
Leu Ile Gly Ser Ala Arg Ala Thr Ile Gln Leu Leu Ser Phe Glu Val
                                 25
             20
Val Ser Thr Leu Thr Ile Leu Ala Pro Leu Met Val Val Gly Ser Leu
        35
                             40
Ser Leu Val Glu Ile Asn His Tyr Gln Ser Gly Gly Phe Leu Asp Trp
                         55
Leu Val Phe Lys Gln Pro Leu Ala Phe Val Leu. Phe Leu Ile Ala Ser
                                         75
Tyr Ala Glu Leu Asn Arg Thr Pro Phe Asp Leu Leu Glu His Glu Ala
                                     90
                 85
Glu Ile Val Ala Gly Tyr Cys Thr Glu Tyr Ser Gly Leu Lys Trp Gly
                                105
                                                    110
Met Phe Phe Leu Ala Glu Tyr Ala His Leu Phe Ala Phe Ser Phe Val
                            120
                                                125
Ile Ser Ile Val Phe Phe Gly Gly Phe Asn Ala Trp Gly Phe Ile Pro
                                            140
    130
                        135
Gly Gly Ile Ala Ile Leu Ile Lys Ala Gly Phe Phe Val Phe Leu Ser
                                        155
                    150
Met Trp Val Arg Ala Thr Tyr Pro His Val Arg Pro Asp Gln Leu Met
                                    170
                165
Asp Met Cys Trp Lys Ile Met Leu Pro Leu Ala Leu Leu Asn Ile Val
                                185
            180
Leu Thr Gly Ile Ile Leu Ile
        195
<210> 21
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<213> Helicobacter pylori
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<221> CDS
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Asp Ala Lys Ala Gln Glu Val Ala Met Cys Val Ala Met Gly Lys Thr
                                     10
                 5
 1
cta aac gat aag ggg cgc ttg aaa cac tcc gtg cat gag ttt tac att
Leu Asn Asp Lys Gly Arg Leu Lys His Ser Val His Glu Phe Tyr Ile
```

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30
                                 25
aaa too coo gaa gaa atg goa aag oto ttt goa gat att ooa gaa got
                                                                   144
Lys Ser Pro Glu Glu Met Ala Lys Leu Phe Ala Asp Ile Pro Glu Ala
                             40
tta gaa aac acc caa gaa atc gct gat aaa tgc gtt tta gag att gat
                                                                   192
Leu Glu Asn Thr Gln Glu Ile Ala Asp Lys Cys Val Leu Glu Ile Asp
                                             60
                         55
tta aaa gac gat aaa aag aac ccc cca acc ccc cca agc ttc aaa ttc
                                                                   240
Leu Lys Asp Asp Lys Lys Asn Pro Pro Thr Pro Pro Ser Phe Lys Phe
                     70
act aaa gct tac gct caa aat gag ggg ctg aat ttt gaa gat gac gct
                                                                   288
Thr Lys Ala Tyr Ala Gln Asn Glu Gly Leu Asn Phe Glu Asp Asp Ala
                                     90
                 85
tot tat tit goo tat aag got aga gaa ggo tig aaa gag ogo tia git
Ser Tyr Phe Ala Tyr Lys Ala Arg Glu Gly Leu Lys Glu Arg Leu Val
                                                     110
                                105
            100
tta gta cca aaa gaa aag cat gat caa tat aaa gag cgc cta gaa aaa
Leu Val Pro Lys Glu Lys His Asp Gln Tyr Lys Glu Arg Leu Glu Lys
                                                 125
                            120
        115
gaa att gaa gtc att acg aac atg aaa ttc cca ggg tat atg ctg att
Glu Ile Glu Val Ile Thr Asn Met Lys Phe Pro Gly Tyr Met Leu Ile
                                             140
                        135
gtg tgg gat ttt atc cgt tat gct aag gaa atg ggc att cct
Val Trp Asp Phe Ile Arg Tyr Ala Lys Glu Met Gly Ile Pro
                     150
 145
 <210> 22
 <211> 158
 <212> PRT
 <213> Helicobacter pylori
 Asp Ala Lys Ala Gln Glu Val Ala Met Cys Val Ala Met Gly Lys Thr
 <400> 22
                                      10
 Leu Asn Asp Lys Gly Arg Leu Lys His Ser Val His Glu Phe Tyr Ile
 Lys Ser Pro Glu Glu Met Ala Lys Leu Phe Ala Asp Ile Pro Glu Ala
 Leu Glu Asn Thr Gln Glu Ile Ala Asp Lys Cys Val Leu Glu Ile Asp
 Leu Lys Asp Asp Lys Lys Asn Pro Pro Thr Pro Pro Ser Phe Lys Phe
                      70
  65
 Thr Lys Ala Tyr Ala Gln Asn Glu Gly Leu Asn Phe Glu Asp Asp Ala
 Ser Tyr Phe Ala Tyr Lys Ala Arg Glu Gly Leu Lys Glu Arg Leu Val
                                                     110
                                 105
 Leu Val Pro Lys Glu Lys His Asp Gln Tyr Lys Glu Arg Leu Glu Lys
                                                 125
                             120
 Glu Ile Glu Val Ile Thr Asn Met Lys Phe Pro Gly Tyr Met Leu Ile
                                             140
                         135
Val Trp Asp Phe Ile Arg Tyr Ala Lys Glu Met Gly Ile Pro
                     150
 145
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 <213> Helicobacter pylori
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 <221> CDS
 <222> (1)..(510)
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 Lys Asn Lys Ala Phe His Asn Ile Ala Leu Asp Ile Glu Thr Leu Asn
                                       10
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caa qaa gcc cta aaa aac act tat gat gtg agc gca atc agc ttt ggg
Gln Glu Ala Leu Lys Asn Thr Tyr Asp Val Ser Ala Ile Ser Phe Gly
                                  25
tta tac cct aaa att qcq aac gat tac gcc tta ctc ccc acg gca acg
Leu Tyr Pro Lys Ile Ala Asn Asp Tyr Ala Leu Leu Pro Thr Ala Thr
                             40
age ttt ggg aat gge tat ggg eet aaa tta gtg aaa aaa aag gge gtg
Ser Phe Gly Asn Gly Tyr Gly Pro Lys Leu Val Lys Lys Lys Gly Val
                         55
aaa ttq aaa aaa gat ttt aga gtc gca tta agt ggg gag cac acc acc
                                                                   240
Lys Leu Lys Lys Asp Phe Arg Val Ala Leu Ser Gly Glu His Thr Thr
                     70
                                         75
                                                                   288
aac gee etc ttg ttt aag ate tat tae aaa eat geg ege ate aet tat
Asn Ala Leu Leu Phe Lys Ile Tyr Tyr Lys His Ala Arg Ile Thr Tyr
                                     90
                 85
atq aat ttt tta gac att gaa aaa gcg gtt ttg gaa gaa aaa gtg cat
                                                                   336
Met Asn Phe Leu Asp Ile Glu Lys Ala Val Leu Glu Glu Lys Val His
            100
                                105
gcg ggc gta ttg atc cat gag agt atc ttg gat ttt cat aat gaa tta
                                                                   384
Ala Gly Val Leu Ile His Glu Ser Ile Leu Asp Phe His Asn Glu Leu
        115
                            120
gaa gtg gaa aaa gaa ttg tgg gat gtt tgg aaa gaa ctc att gaa gtg
Glu Val Glu Lys Glu Leu Trp Asp Val Trp Lys Glu Leu Ile Glu Val
                        135
gat ttg ccc ttg cct tta ggg ggc atg gcg atc agg cga tct atc ccc
Asp Leu Pro Leu Pro Leu Gly Gly Met Ala Ile Arg Arg Ser Ile Pro
                    150
145
ttg tat cgc gcg att ttg att aaa aag gct tt
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Leu Tyr Arg Ala Ile Leu Ile Lys Lys Ala
                165
<210> 24
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<212> PRT
<213> Helicobacter pylori
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Lys Asn Lys Ala Phe His Asn Ile Ala Leu Asp Ile Glu Thr Leu Asn
Gln Glu Ala Leu Lys Asn Thr Tyr Asp Val Ser Ala Ile Ser Phe Gly
Leu Tyr Pro Lys Ile Ala Asn Asp Tyr Ala Leu Leu Pro Thr Ala Thr
Ser Phe Gly Asn Gly Tyr Gly Pro Lys Leu Val Lys Lys Gly Val
Lys Leu Lys Lys Asp Phe Arg Val Ala Leu Ser Gly Glu His Thr Thr
                     70
Asn Ala Leu Leu Phe Lys Ile Tyr Tyr Lys His Ala Arg Ile Thr Tyr
                                     90
Met Asn Phe Leu Asp Ile Glu Lys Ala Val Leu Glu Glu Lys Val His
                                105
Ala Gly Val Leu Ile His Glu Ser Ile Leu Asp Phe His Asn Glu Leu
                            120
Glu Val Glu Lys Glu Leu Trp Asp Val Trp Lys Glu Leu Ile Glu Val
                                            140
                        135
Asp Leu Pro Leu Pro Leu Gly Gly Met Ala Ile Arg Arg Ser Ile Pro
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                                        155
Leu Tyr Arg Ala Ile Leu Ile Lys Lys Ala
               165
<210> 25
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<212> DNA
<213> Helicobacter pylori
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<221> CDS
<222> (1)..(432)
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<400> 25
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Leu Lys Ile Ile Gln Gly Ala Leu Asp Thr Arg Glu Leu Leu Lys Ala
                                     10
                  5
tac caa gag gaa gct tgc gcg aaa aac ttt gga gcg ttt tgt gtg ttt
                                                                   96
Tyr Gln Glu Glu Ala Cys Ala Lys Asn Phe Gly Ala Phe Cys Val Phe
                                 25
             20
gtg ggg att gtg aga aaa gag gat aac att caa ggc ttg agt ttt gat
                                                                   144
Val Gly Ile Val Arg Lys Glu Asp Asn Ile Gln Gly Leu Ser Phe Asp
                             40
         35
att tat gaa gcg cta tta aag act tgg ttt gaa aaa tgg cac cat aaa
                                                                   192
Ile Tyr Glu Ala Leu Leu Lys Thr Trp Phe Glu Lys Trp His His Lys
                                              60
                         55
gcc aaa gat ttg ggc gtg gtg tta aaa atg gcg cac agc ctg ggc gat
                                                                   240
Ala Lys Asp Leu Gly Val Val Leu Lys Met Ala His Ser Leu Gly Asp
                                         75
                     70
gtt ttg ata gga caa agc tca ttt tta tgc gtt tca atg gga aag aat
                                                                   288
Val Leu Ile Gly Gln Ser Ser Phe Leu Cys Val Ser Met Gly Lys Asn
                                                          95
                                     90
                 85
aga aaa aat gcc tta gaa cta tac gaa aat ttt att gaa gat ttt aag
                                                                   336
Arg Lys Asn Ala Leu Glu Leu Tyr Glu Asn Phe Ile Glu Asp Phe Lys
                                105
            100
cat aac gct cct att tgg aaa tac gat tta atc cat aat aaa cgc att
                                                                   384
His Asn Ala Pro Ile Trp Lys Tyr Asp Leu Ile His Asn Lys Arg Ile
                                                 125
                            120
        115
tat gct aaa gaa aga agc cac cct tta aaa ggg agc ggg ctt tta gct
                                                                   432
Tyr Ala Lys Glu Arg Ser His Pro Leu Lys Gly Ser Gly Leu Leu Ala
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                         135
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<210> 26
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 <213> Helicobacter pylori
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 Leu Lys Ile Ile Gln Gly Ala Leu Asp Thr Arg Glu Leu Leu Lys Ala
                                      10
 Tyr Gln Glu Glu Ala Cys Ala Lys Asn Phe Gly Ala Phe Cys Val Phe
  1
                                  25
              20
 Val Gly Ile Val Arg Lys Glu Asp Asn Ile Gln Gly Leu Ser Phe Asp
                              40
          35
 Ile Tyr Glu Ala Leu Leu Lys Thr Trp Phe Glu Lys Trp His His Lys
                          55
      50
 Ala Lys Asp Leu Gly Val Val Leu Lys Met Ala His Ser Leu Gly Asp
                      70 .
 Val Leu Ile Gly Gln Ser Ser Phe Leu Cys Val Ser Met Gly Lys Asn
                                      90
                  85
 Arg Lys Asn Ala Leu Glu Leu Tyr Glu Asn Phe Ile Glu Asp Phe Lys
                                 105
             100
 His Asn Ala Pro Ile Trp Lys Tyr Asp Leu Ile His Asn Lys Arg Ile
                                                 125
                             120
 Tyr Ala Lys Glu Arg Ser His Pro Leu Lys Gly Ser Gly Leu Leu Ala
                         135
     130
 <210> 27
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 <212> DNA
 <213> Helicobacter pylori
 <220>
 <221> CDS
 <222> (1)..(516)
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1400	1 2	,														
)> 27 agc		age	aca	gat	aaa	ttc	ttt	aac	aσt	aca	caa	aca	aac	att	48
Leu	Ser	Phe	Ser	Ala	Asp	Lys	Phe	Phe	Asn	Ser	Ala	Gln	Ala	ĞÎy	Ile	
1				5					10					15		
att	atg	ggg	caa	aaa	gaa	cgg	gtt	gaa	gcg	tta	aaa	aac	cac	ccc	ctt	96
Ile	Met	Gly	Gln	Lys	Glu	Arg	Val		Ala	Leu	Lys	Asn		Pro	Leu	
			20					25					30			144
tat	aga	gtt	tta	agg	gtg	ggt	aaa	atc	acg	CtC	acc	ttg	CEE	Dho	Cuc	144
Tyr	Arg		Leu	Arg	vaı	GIA	40	116	1111	nea	IIII	45	Leu	FIIC	Cys	
300	cta	35	aca	taa	ata	aat		caa	gaa	gac	att		atc	cat	aca	192
Ser	Leu	T.vs	Ala	Tro	Ile	Asn	His	Gln	Glu	Asp	Ile	Thr	Ile	His	Ala	
001	50	2,0				55				•	60					
tta	ttg	aac	caa	act	aaa	gac	gca	tta	ttg	caa	aaa	gcc	ctc	aaa	ctc	240
Leu	Leu	Asn	Gln	Thr	Lys	Asp	Ala	Leu	Leu		Lys	Ala	Leu	Lys		
65					70					75					80	200
tac	gct Ala	ctt	tta	aag	cct	tta	gaa	ttg	aat	gtg	agc	ata	gcc Ala	CCC	agc	288
Tyr	АТА	Leu	Leu	ьуs 85	Pro	Leu	GIU	Leu	90	AGT	Ser	TIC	AIG	95	Ser	
+++	tct	aaa	ata		aat	tta	ttt	aat		gaa	tta	qaa	tcc		tqc	336
Phe	Ser	Lvs	Ile	Gly	Asn	Leu	Phe	Gly	Arg	Ğlu	Leu	Ğlu	Ser	Phe	Cys	
		_	100	_				105					110			
gtg	aaa	atc	cag	ccc	aaa	aac	acc	cgt	gct	tta	aat	agt	gag	aaa	ctt	384
Val	Lys		Gln	Pro	Lys	Asn		Arg	Ala	Leu	Asn		Glu	Lys	Leu	
		115					120		-+-	~~~	200	125	+00	+ ~ ~	~ 22	432
tat	tta Leu	aag	CEE	Dho	Caa	Luc	Glv	Val	Tle	Ala	Ara	Tle	Ser	Cvs	Glu	432
Tyr	130	гуз	Den	1116	GIII	135	O.T.J				140			-,-		
ttc	ata	tqc	ttt	qaa	gtc	ttt	agc	ttg	aat	gạa	aaa	gat	ttt	gaa	aaa	480
Phe	Val	Cys	Phe	Ğlu	Val	Phe	Ser	Leu	Asn	Glu.	Lys	Asp	Phe	Glu	Lys	
145		_		•	150					155					160	
atc	gct	ctg	gtt	tta	gaa	gaa	att	ctt	aat	aaa	gct					516
Ile	Ala	Leu	Val	_	Glu	Glu	Ile	Leu	170	гÀз	Ala					
-216)> 28	3		165					170							
	1> 1															
	2> PI															
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<40)> 21	3	_		_	_		_,	•	0		C1	81-	C1	71.	
_	Ser	Phe	Ser	Ala	Asp	Lys	Phe	Pne	Asn 10	Ser	AIa	GIN	ATA	15	11e	
1	Met	C1	Gln	Tue	Glu	Ara	Val	Glu		ī.en	T.vs	Asn	His		Leu	
ire	Met	GIY		БУЗ									30			
Tvr	Arg	Val							Thr	Leu	Thr	Leu		Phe	Cys	
-	_	35					40					45				
Ser	Leu	Lys	Ala	Trp	Ile		His	Gln	Glu	Asp		Thr	Ile	His	Ala	
	50					55					60					
		_			_			•	•	61 -			T	*	T	
	Leu	Asn	Gln	Thr			Ala	Leu	Leu	Gln 75		Ala	Leu	Lys		
65					70	Asp				75	Lys				80	
65	Leu Ala			Lys	70	Asp			Asn	75	Lys				80	
65 Tyr	Ala	Leu	Leu	Lys 85	70 Pro	Asp Leu	Glu	Leu	Asn 90	75 Val	Lys Ser	Ile	Ala	Ser 95	80 Ser	
65 Tyr Phe	Ala Ser	Leu Lys	Leu Ile 100	Lys 85 Gly	70 Pro Asn	Asp Leu Leu	Glu Phe	Leu Gly 105	Asn 90 Arg	75 Val Glu	Lys Ser Leu	Ile Glu	Ala Ser 110	Ser 95 Phe	80 Ser Cys	
65 Tyr Phe	Ala	Leu Lys	Leu Ile 100	Lys 85 Gly	70 Pro Asn	Asp Leu Leu	Glu Phe	Leu Gly 105	Asn 90 Arg	75 Val Glu	Lys Ser Leu	Ile Glu Ser	Ala Ser 110	Ser 95 Phe	80 Ser Cys	
65 Tyr Phe Val	Ala Ser Lys	Leu Lys Ile 115	Leu Ile 100 Gln	Lys 85 Gly Pro	70 Pro Asn Lys	Asp Leu Leu Asn	Glu Phe Thr 120	Leu Gly 105 Arg	Asn 90 Arg Ala	75 Val Glu Leu	Lys Ser Leu Asn	Ile Glu Ser 125	Ala Ser 110 Glu	Ser 95 Phe Lys	80 Ser Cys Leu	
65 Tyr Phe Val	Ala Ser Lys Leu	Leu Lys Ile 115	Leu Ile 100 Gln	Lys 85 Gly Pro	70 Pro Asn Lys	Asp Leu Leu Asn	Glu Phe Thr 120	Leu Gly 105 Arg	Asn 90 Arg Ala	75 Val Glu Leu	Lys Ser Leu Asn Arg	Ile Glu Ser 125	Ala Ser 110 Glu	Ser 95 Phe Lys	80 Ser Cys Leu	
65 Tyr Phe Val Tyr	Ala Ser Lys Leu 130	Leu Lys Ile 115 Lys	Leu Ile 100 Gln Leu	Lys 85 Gly Pro	70 Pro Asn Lys Gln	Asp Leu Leu Asn Lys 135	Glu Phe Thr 120 Gly	Leu Gly 105 Arg Val	Asn 90 Arg Ala Ile	75 Val Glu Leu Ala	Lys Ser Leu Asn Arg 140	Ile Glu Ser 125 Ile	Ala Ser 110 Glu Ser	Ser 95 Phe Lys Cys	80 Ser Cys Leu Glu	
65 Tyr Phe Val Tyr	Ala Ser Lys Leu	Leu Lys Ile 115 Lys	Leu Ile 100 Gln Leu	Lys 85 Gly Pro	70 Pro Asn Lys Gln Val	Asp Leu Leu Asn Lys 135	Glu Phe Thr 120 Gly	Leu Gly 105 Arg Val	Asn 90 Arg Ala Ile	75 Val Glu Leu Ala Glu	Lys Ser Leu Asn Arg 140	Ile Glu Ser 125 Ile	Ala Ser 110 Glu Ser	Ser 95 Phe Lys Cys	80 Ser Cys Leu Glu	
65 Tyr Phe Val Tyr Phe 145	Ala Ser Lys Leu 130 Val	Leu Lys Ile 115 Lys	Leu Ile 100 Gln Leu Phe	Lys 85 Gly Pro Phe Glu	70 Pro Asn Lys Gln Val 150	Asp Leu Leu Asn Lys 135 Phe	Glu Phe Thr 120 Gly Ser	Leu Gly 105 Arg Val Leu	Asn 90 Arg Ala Ile Asn	75 Val Glu Leu Ala Glu 155	Lys Ser Leu Asn Arg 140 Lys	Ile Glu Ser 125 Ile	Ala Ser 110 Glu Ser	Ser 95 Phe Lys Cys	80 Ser Cys Leu Glu	
65 Tyr Phe Val Tyr Phe 145	Ala Ser Lys Leu 130	Leu Lys Ile 115 Lys	Leu Ile 100 Gln Leu Phe	Lys 85 Gly Pro Phe Glu	70 Pro Asn Lys Gln Val 150	Asp Leu Leu Asn Lys 135 Phe	Glu Phe Thr 120 Gly Ser	Leu Gly 105 Arg Val Leu	Asn 90 Arg Ala Ile Asn	75 Val Glu Leu Ala Glu 155	Lys Ser Leu Asn Arg 140 Lys	Ile Glu Ser 125 Ile	Ala Ser 110 Glu Ser	Ser 95 Phe Lys Cys	80 Ser Cys Leu Glu	

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atc att act caa gct aga aag gct aat ggg gtg att gtt cta gcc tta
Ile Ile Thr Gln Ala Arg Lys Ala Asn Gly Val Ile Val Leu Ala Leu
                                     10
caa gac att aac caa cta agc gaa gtg aga aac gct caa agc ttt ata
                                                                   96
Gln Asp Ile Asn Gln Leu Ser Glu Val Arg Asn Ala Gln Ser Phe Ile
                                 25
             20
aaa aat atg ggg caa ttg att ttg tat ccc caa aga aat att gat acc
Lys Asn Met Gly Gln Leu Ile Leu Tyr Pro Gln Arg Asn Ile Asp Thr
                             40
aaa gat tta aac gat aaa ttt ggc att aga cta agc gat aca gaa aaa
                                                                   192
Lys Asp Leu Asn Asp Lys Phe Gly Ile Arg Leu Ser Asp Thr Glu Lys
                         55
cat ttt tta gaa aac acc gcc gtt aat gaa tac aaa gtc tta ctc aaa
                                                                   240
His Phe Leu Glu Asn Thr Ala Val Asn Glu Tyr Lys Val Leu Leu Lys
                     70
aac atg aat gat ggc tca tct aac att ata gat gtg agc cta agt tct
                                                                    288
Asn Met Asn Asp Gly Ser Ser Asn Ile Ile Asp Val Ser Leu Ser Ser
                 85
ttg ggt aat tac cta caa atc ttt agc tct aat tct agc atg gta gaa
                                                                    336
Leu Gly Asn Tyr Leu Gln Ile Phe Ser Ser Asn Ser Ser Met Val Glu
                                 105
            100
cac att gat aat ctc att aag cat tac cct aaa act tgg cga gaa gtc
                                                                    384
His Ile Asp Asn Leu Ile Lys His Tyr Pro Lys Thr Trp Arg Glu Val
                                                 125
                            120
        115
ttt gtg agt aac aaa cac gaa aat ttt gat gac aaa aaa cac tta gaa
Phe Val Ser Asn Lys His Glu Asn Phe Asp Asp Lys Lys His Leu Glu
                         135
    130
                                                                    444
aag gtg ctt aaa
Lys Val Leu Lys
145
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 <213> Helicobacter pylori
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Ile Ile Thr Gln Ala Arg Lys Ala Asn Gly Val Ile Val Leu Ala Leu
                                      10
Gln Asp Ile Asn Gln Leu Ser Glu Val Arg Asn Ala Gln Ser Phe Ile
Lys Asn Met Gly Gln Leu Ile Leu Tyr Pro Gln Arg Asn Ile Asp Thr
 Lys Asp Leu Asn Asp Lys Phe Gly Ile Arg Leu Ser Asp Thr Glu Lys
                          55
 His Phe Leu Glu Asn Thr Ala Val Asn Glu Tyr Lys Val Leu Leu Lys
                                          75
                      70
Asn Met Asn Asp Gly Ser Ser Asn Ile Ile Asp Val Ser Leu Ser Ser
                                      90
                  85
 Leu Gly Asn Tyr Leu Gln Ile Phe Ser Ser Asn Ser Ser Met Val Glu
                                 105
 His Ile Asp Asn Leu Ile Lys His Tyr Pro Lys Thr Trp Arg Glu Val
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                            120
 Phe Val Ser Asn Lys His Glu Asn Phe Asp Asp Lys Lys His Leu Glu
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                         135
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Lys Val Leu Lys
145
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<213> Helicobacter pylori
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Thr Val Gly Asp Val Phe Gly Glu Asn Gly Leu Leu Asn Ala Leu Asp
                                     .10
cct acg gaa aga aaa aat gat caa atg ctt tta gag caa atc caa
                                                                   96
Pro Thr Glu Arg Lys Lys Ile Asp Gln Met Leu Leu Glu Gln Ile Gln
                                 25
gcc cat tct tca ggg ttt gaa aaa ttc atc gtg aaa act tta ggg att
                                                                   144
Ala His Ser Ser Gly Phe Glu Lys Phe Ile Val Lys Thr Leu Gly Ile
                             40
         35
gaa aat gta gag aat ttc atc aat aac tgg tat ggc aag caa agc ttg
                                                                   192
Glu Asn Val Glu Asn Phe Ile Asn Asn Trp Tyr Gly Lys Gln Ser Leu
                                             60
                         55
agt tot ttt gcc aat aat ttt gtg cot gga ggc ttg aat caa gcc ctt
                                                                   240
Ser Ser Phe Ala Asn Asn Phe Val Pro Gly Gly Leu Asn Gln Ala Leu
                                         75
                     70
gat aaa ata ggc tct agc tct gat gcc aaa gac tta cag aac ttc ttg
                                                                   288
Asp Lys Ile Gly Ser Ser Ser Asp Ala Lys Asp Leu Gln Asn Phe Leu
                                     90
                 85
gat aaa acg act ttt ggg gat att tta aat caa atg att gaa caa gcc
                                                                   336
Asp Lys Thr Thr Phe Gly Asp Ile Leu Asn Gln Met Ile Glu Gln Ala
                                                    110
                               105
            100
ccc tta atc aat aaa ctc att tct tgg ctg ggt ccg cag gat ttg agc
                                                                   384
Pro Leu Ile Asn Lys Leu Ile Ser Trp Leu Gly Pro Gln Asp Leu Ser
                                                 125
                            120
        115
gtt tta gtg aat atc gct tta aat agc atc act aac cct agt
                                                                   426
Val Leu Val Asn Ile Ala Leu Asn Ser Ile Thr Asn Pro Ser
    130
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<213> Helicobacter pylori
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Thr Val Gly Asp Val Phe Gly Glu Asn Gly Leu Leu Asn Ala Leu Asp
Pro Thr Glu Arg Lys Lys Ile Asp Gln Met Leu Leu Glu Gln Ile Gln
             20
Ala His Ser Ser Gly Phe Glu Lys Phe Ile Val Lys Thr Leu Gly Ile
                             40
Glu Asn Val Glu Asn Phe Ile Asn Asn Trp Tyr Gly Lys Gln Ser Leu
                                              60
Ser Ser Phe Ala Asn Asn Phe Val Pro Gly Gly Leu Asn Gln Ala Leu
                                         75
Asp Lys Ile Gly Ser Ser Ser Asp Ala Lys Asp Leu Gln Asn Phe Leu
                                      90
                 85
Asp Lys Thr Thr Phe Gly Asp Ile Leu Asn Gln Met Ile Glu Gln Ala
                                                     110
                                105
Pro Leu Ile Asn Lys Leu Ile Ser Trp Leu Gly Pro Gln Asp Leu Ser
                                                 125
                            120
Val Leu Val Asn Ile Ala Leu Asn Ser Ile Thr Asn Pro Ser
    130
                        135
<210> 33
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<213> Helicobacter pylori
<220>
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Gln Ala His His Leu Lys Asn Leu Leu Glu Ala Phe Tyr His Gln Asn
                                     10
aaa gag agt ttg ggc ttt ttt tcc cct tat ttt agt ttg cga tct caa
                                                                   96
Lys Glu Ser Leu Gly Phe Phe Ser Pro Tyr Phe Ser Leu Arg Ser Gln
                                 25
             20
acc cet age gte tet tat gaa age geg tta get tet tta gaa aac tat
Thr Pro Ser Val Ser Tyr Glu Ser Ala Leu Ala Ser Leu Glu Asn Tyr
                             40
        35
ttt atg get ttg ttc caa tcc cat ttt aaa gac gat acc gea etc caa
                                                                   192
Phe Met Ala Leu Phe Gln Ser His Phe Lys Asp Asp Thr Ala Leu Gln
                         55
cag aat ttt aaa gga ttg ttg caa gcc ttt gtt tct atg gct aaa gac
                                                                   240
Gln Asn Phe Lys Gly Leu Leu Gln Ala Phe Val Ser Met Ala Lys Asp
                                         75 '
                     70
aaa cga tcc caa atc gct ctt aac gcc caa gct aaa gac aac gcc aag
                                                                   288
Lys Arg Ser Gln Ile Ala Leu Asn Ala Gln Ala Lys Asp Asn Ala Lys
                                     90
                 85
cta act ttt aac gcc ttg tta gaa agc ctt agc gtg aat ttc ttt caa
                                                                   336
Leu Thr Phe Asn Ala Leu Leu Glu Ser Leu Ser Val Asn Phe Phe Gln
                                105
            100
                                                                   357
tct tac aaa ata agc cat gag
Ser Tyr Lys Ile Ser His Glu
        115
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<213> Helicobacter pylori
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Gln Ala His His Leu Lys Asn Leu Leu Glu Ala Phe Tyr His Gln Asn
                                      10
                  5
Lys Glu Ser Leu Gly Phe Phe Ser Pro Tyr Phe Ser Leu Arg Ser Gln
                                  25
             20
Thr Pro Ser Val Ser Tyr Glu Ser Ala Leu Ala Ser Leu Glu Asn Tyr
                              40
         35
Phe Met Ala Leu Phe Gln Ser His Phe Lys Asp Asp Thr Ala Leu Gln
                          55
Gln Asn Phe Lys Gly Leu Leu Gln Ala Phe Val Ser Met Ala Lys Asp
                                          75
                      70
Lys Arg Ser Gln Ile Ala Leu Asn Ala Gln Ala Lys Asp Asn Ala Lys
                                      90
Leu Thr Phe Asn Ala Leu Leu Glu Ser Leu Ser Val Asn Phe Phe Gln
                                 105
             100
Ser Tyr Lys Ile Ser His Glu
        115
<210> 35
<211> 980
<212> - DNA
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<221> CDS
<222> (1)..(978)
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gtg ggt tot gga gcc ggg agg aaa gcc agc tot acg gtt tta act ttg
```

WO 00/66722 PCT/IB00/00603

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1	Gly			5					10					15		
caa	gct	tca	qaa	qqq	att	act	agc	agt	aaa	aat	gcg	gaa	att	tct	ctt	96
Gln	Ala	Ser	Glu 20	Gly	Ile	Thr	Ser	Ser 25	Lys	Asn	Ala	Glu	Ile 30	Ser	Leu	
tat	gat	ggc	gcc	acg	ctc	aat	ttg	gct	tca	aac	agc	gtt	aaa	tta	atg	144
Tyr	Asp	Gly 35	Ala	Thr	Leu	Asn	Leu 40	Ala	Ser	Asn	Ser	Val 45	Lys	Leu	Met	• • • •
ggt	aat	gtg	tgg	atg	ggc	cgt	ttg	caa	tat	gtg	gga	gcg	tat	ttg	gcc	192
_	Asn 50					55					60					
cct	tca	tac	agc	acg	ata	aac	act	tca	aaa	gtg	aca	ggg	gaa	gtg	aat	240
65	Ser				70					75					80	200
ttt	aac	cat	ctc	act	gtg	ggc	gat	cac	aac	gcc	gct	caa	gca	ggc	att	288
	Asn			85					90					95		326
atc	gct	agt	aac	aag	act	cat	att	ggc	aca	ctg	gat	ttg	Egg	caa	agc	336
	Ala		100					105					110			204
gcg	gga	cta	aac	att	atc	gcc	CCT	cca	gaa	ggc	ggt	Lat.	aag	yac	Tara	384
	Gly	115					120					125				432
cct	aag	gat	aaa	CCT	agt	aac	acc	acg	Caa	aat Nee	nac non	Ala	Acr.	Acr.	Aco	7.72
	Lys 130	-				135					140					480
caa	caa Gln	aac	agc	gct	Caa	aac aac	Aac Non	Cor	Acn	Thr	Gln	Val	Tle	Acn	Pro	100
	GIN	Asn	Ser	Ala		ASII	ASII	Ser	No!!	155	GIII	Val	110	7311	160	
145	aat				150		~~~	-++	000		3 C C	C22	atc	att		528
ccc	aat Asn	agc	gcg	Caa	add	The	Clu	Tlo	Cla	Dro	Thr	Gla	Val	Tle	Asn	720
	cct			165					170					175		576
999	Pro	Dho	NI.	Glu	Glv	Lve	Aen	Thr	Val	Val	Asn	Tle	Asp	Ara	Ile	• • •
_	act		180					185					190			624
Nan	Thr	Aen	Mla	Agn	Glv	Thr	Ile	Lvs	Val	ĞĨv	ĞÎv	Tvr	Lvs	Åla	Ser	
	acc	195					200					205				672
Len	Thr	Thr	Asn	Ala	Ala	His	Leu	His	Ile	Gly	Lys	Gly	Gly	Ile	Asn	
	210 tcc					215					220					720
tou	Ser	Acn	Gln	Ala	Ser	Glv	Ara	Thr	Leu	Leu	Val	Ğlu	Asn	Leu	Thr	
	Ser	ASII	GIII	VIG	230	GIJ	9	••••		235					240	
225	aat	2+0	200	att		aaa	cct	tta	aga		aat	aat	caa	ata		768
Gly	Asn	Ile	Thr	Val 245	Asp	Gly	Pro	Leu	Arg 250	Val	Asn	Asn	Gln	Val 255	GTA	
aat	tat	act	ttq	qca	gga	tca	agc	gcg	aat	ttt	gag	ttt	aag	gct	ggt	816
Gly	Tyr	Ala	Leu 260	Ala	Gly	Ser	Ser	Ala 265	Asn	Phe	Glu	Phe	Lys 270	Ala	Gly	
acq	gat	acc	aaa	aac	ggc	aca	gcc	act	ttt	aat	aac	gat	att	agt	ttg	864
Thr	Asp	Thr 275	Lys	Asn	Gly	Thr	Ala 280	Thr	Phe	Asn	Asn	Asp 285	Ile	Ser	Leu	
gga	aga	ttt	qtq	aat	tta	aaa	gtg	gat	gct	cat	aca	gct	aat	ttt	aaa	912
Gly	Arg 290	Phe	Val	Asn	Leu	Lys 295	Val	Asp	Ala	His	Thr 300	Ala	Asn	Phe	Lys	
gat	att	gat	act	gat	aat	ggt	ggt	ttc	aac	acc	tta	gat	ttt	agt	ggc	960
Gly 305	Ile	Asp	Thr	Gly	Asn 310	ĞÎy	Ğĺy	Phe	Asn	Thr 315	Leu	Asp	Phe	Ser	Gly 320	
	aca	gat	aao	gtc		at					•					980
Val	Thr	Gly	Lys	Val	Asn											

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Val Gly Ser Gly Ala Gly Arg Lys Ala Ser Ser Thr Val Leu Thr Leu
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Tyr Asp Gly Ala Thr Leu Asn Leu Ala Ser Asn Ser Val Lys Leu Met
                             40
        35
Gly Asn Val Trp Met Gly Arg Leu Gln Tyr Val Gly Ala Tyr Leu Ala
                       55
Pro Ser Tyr Ser Thr Ile Asn Thr Ser Lys Val Thr Gly Glu Val Asn
                                        75
                    70
Phe Asn His Leu Thr Val Gly Asp His Asn Ala Ala Gln Ala Gly Ile
                                    90
                 85
Ile Ala Ser Asn Lys Thr His Ile Gly Thr Leu Asp Leu Trp Gln Ser
                                                  110
                       . 105
            100
Ala Gly Leu Asn Ile Ile Ala Pro Pro Glu Gly Gly Tyr Lys Asp Lys
                                                125
                           120
Pro Lys Asp Lys Pro Ser Asn Thr Thr Gln Asn Asn Ala Asn Asn Asn
        115
                                            140
                       135
Gln Gln Asn Ser Ala Gln Asn Asn Ser Asn Thr Gln Val Ile Asn Pro
    130
                                        155
                   150
Pro Asn Ser Ala Gln Lys Thr Glu Ile Gln Pro Thr Gln Val Ile Asp
                                                        175
                                    170
                165
Gly Pro Phe Ala Gly Gly Lys Asp Thr Val Val Asn Ile Asp Arg Ile
                                                   190
                                185
           180
Asn Thr Asn Ala Asp Gly Thr Ile Lys Val Gly Gly Tyr Lys Ala Ser
                                                205
                            200
 . 195
Leu Thr Thr Asn Ala Ala His Leu His Ile Gly Lys Gly Gly Ile Asn
                                            220
                        215
Leu Ser Asn Gln Ala Ser Gly Arg Thr Leu Leu Val Glu Asn Leu Thr
                                       235
                    230
 Gly Asn Ile Thr Val Asp Gly Pro Leu Arg Val Asn Asn Gln Val Gly
                                    250
                245
 Gly Tyr Ala Leu Ala Gly Ser Ser Ala Asn Phe Glu Phe Lys Ala Gly
                                                   270
                                265
 Thr Asp Thr Lys Asn Gly Thr Ala Thr Phe Asn Asn Asp Ile Ser Leu
                                               285
                            280
         275
 Gly Arg Phe Val Asn Leu Lys Val Asp Ala His Thr Ala Asn Phe Lys
                                            300
                       295
 Gly Ile Asp Thr Gly Asn Gly Gly Phe Asn Thr Leu Asp Phe Ser Gly
                                        315
                   310
 Val Thr Gly Lys Val Asn
                 325
 <210> 37
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 <213> Helicobacter pylori
 <220>
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 agt aat tta tgt ggt aat ggt agt agc ggt agt agt ggc act act tgc
 Ser Asn Leu Cys Gly Asn Gly Ser Ser Gly Ser Ser Gly Thr Thr Cys
                                     10
 tee ggt tgg ett ate aac ett tta ggg gea ate eee ace aat gga gtg
 Ser Gly Trp Leu Ile Asn Leu Leu Gly Ala Ile Pro Thr Asn Gly Val
```

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20
                                  25
age gat acg aat aat tta att aat etg etc act gaa tte att aaa acc
                                                                   144
Ser Asp Thr Asn Asn Leu Ile Asn Leu Leu Thr Glu Phe Ile Lys Thr
                              40
gcc ggg ttt atc caa aat aat gat agt agt gta tct act agt ctt aca
                                                                   192
Ala Gly Phe Ile Gln Asn Asn Asp Ser Ser Val Ser Thr Ser Leu Thr
                         55
                                              60
age get ttt caa gee att aeg age get att tet caa ggg ttt caa gee
                                                                   240
Ser Ala Phe Gln Ala Ile Thr Ser Ala Ile Ser Gln Gly Phe Gln Ala
                     70
                                          75
tta caa aac gat att agc cct aat gcg att tta acc ttg ctc caa gag
                                                                   288
Leu Gln Asn Asp Ile Ser Pro Asn Ala Ile Leu Thr Leu Leu Gln Glu
                                      90.
                 85
att act tot aac acc acc act cag toa tto tog caa acc tta cgg
                                                                   336
Ile Thr Ser Asn Thr Thr Thr Ile Gln Ser Phe Ser Gln Thr Leu Arg
                                105
            100
cag ctt tta ggg gat aaa aca ttc tt
                                                                   362
Gln Leu Leu Gly Asp Lys Thr Phe
        115
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Ser Asn Leu Cys Gly Asn Gly Ser Ser Gly Ser Ser Gly Thr Thr Cys
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Ser Gly Trp Leu Ile Asn Leu Leu Gly Ala Ile Pro Thr Asn Gly Val
                                 25
             20
Ser Asp Thr Asn Asn Leu Ile Asn Leu Leu Thr Glu Phe Ile Lys Thr
                            . 40
Ala Gly Phe Ile Gln Asn Asn Asp Ser Ser Val Ser Thr Ser Leu Thr
                         55
                                              60
Ser Ala Phe Gln Ala Ile Thr Ser Ala Ile Ser Gln Gly Phe Gln Ala
                     70
                                         75
Leu Gln Asn Asp Ile Ser Pro Asn Ala Ile Leu Thr Leu Leu Gln Glu
                                     90
                 85
Ile Thr Ser Asn Thr Thr Ile Gln Ser Phe Ser Gln Thr Leu Arg
                                105
            100
Gln Leu Leu Gly Asp Lys Thr Phe
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                                                                   48
Leu Phe Ala Asp Ile Pro Glu Ala Leu Glu Asn Thr Gln Glu Ile Ala
                                     10
gat aaa tgc gtt tta gag att gat tta aaa gac gat aaa aag aac ccc
                                                                   96
Asp Lys Cys Val Leu Glu Ile Asp Leu Lys Asp Asp Lys Lys Asn Pro
            20
                                 25
cca acc ccc cca agc ttc aaa ttc act aaa gct tac gct caa aat gag
                                                                   144
Pro Thr Pro Pro Ser Phe Lys Phe Thr Lys Ala Tyr Ala Gln Asn Glu
        35
qqq ctq aat ttt gaa gat gac gct tct tat ttt gcc tat aag gct aga
                                                                   192
Gly Leu Asn Phe Glu Asp Asp Ala Ser Tyr Phe Ala Tyr Lys Ala Arg
                         55
gaa ggc ttg aaa gag cgc tta gtt tta gta cca aaa gaa aag cat gat
```

```
Glu Gly Leu Lys Glu Arg Leu Val Leu Val Pro Lys Glu Lys His Asp
                                          75
                     70
caa tat aaa gag cgc cta gaa aaa gaa att gaa gtc att acg aac atg
                                                                   288
Gln Tyr Lys Glu Arg Leu Glu Lys Glu Ile Glu Val Ile Thr Asn Met
                                      90
                 85
aaa ttc cca ggg tat atg ctg att gtg tgg gat ttt atc cgt tat gct
                                                                   336
Lys Phe Pro Gly Tyr Met Leu Ile Val Trp Asp Phe Ile Arg Tyr Ala
                                                     110
                                105
            100
aag gaa atg ggc att cct gta ggg cct ggt agg ggg agt gcg gcc ggg
                                                                   384
Lys Glu Met Gly Ile Pro Val Gly Pro Gly Arg Gly Ser Ala Ala Gly
                                                 125
                            120
        115
age ttg gtg get ttt get tta aaa ate acg gat att gae eet ttg aaa
                                                                    432
Ser Leu Val Ala Phe Ala Leu Lys Ile Thr Asp Ile Asp Pro Leu Lys
                        135
    130
                                                                    448
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Tyr Asp Leu Leu Phe
145
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<213> Helicobacter pylori
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Asp Lys Cys Val Leu Glu Ile Asp Leu Lys Asp Asp Lys Lys Asn Pro
             20
Pro Thr Pro Pro Ser Phe Lys Phe Thr Lys Ala Tyr Ala Gln Asn Glu
                                                  45.
         35
Gly Leu Asn Phe Glu Asp Asp Ala Ser Tyr Phe Ala Tyr Lys Ala Arg
                          55
Glu Gly Leu Lys Glu Arg Leu Val Leu Val Pro Lys Glu Lys His Asp
                                          75
                      70
Gln Tyr Lys Glu Arg Leu Glu Lys Glu Ile Glu Val Ile Thr Asn Met
 65
                                      90
Lys Phe Pro Gly Tyr Met Leu Ile Val Trp Asp Phe Ile Arg Tyr Ala
                                 105
             100
 Lys Glu Met Gly Ile Pro Val Gly Pro Gly Arg Gly Ser Ala Ala Gly
                                                 125
                             120
 Ser Leu Val Ala Phe Ala Leu Lys Ile Thr Asp Ile Asp Pro Leu Lys
                                             140
                         135
 Tyr Asp Leu Leu Phe
 145
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                                                                    48
 Gln Tyr Asp Phe Lys Ala Met Phe Thr Pro Leu Ile Met Gln Ala Gln
                                      10
 ttg agc tta aga aac att gat aat ttt gtg gaa aaa ggc tct gct ttg
 Leu Ser Leu Arg Asn Ile Asp Asn Phe Val Glu Lys Gly Ser Ala Leu
                                  25
 ata gat aaa ttt gac gct aac ccc tat aaa acg att ttt gga gaa agg
 Ile Asp Lys Phe Asp Ala Asn Pro Tyr Lys Thr Ile Phe Gly Glu Arg
                              40
                                                                    147
 aaa
 Lys
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<210> 42
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<213> Helicobacter pylori
<400> 42
Gln Tyr Asp Phe Lys Ala Met Phe Thr Pro Leu Ile Met Gln Ala Gln
                                     10
Leu Ser Leu Arg Asn Ile Asp Asn Phe Val Glu Lys Gly Ser Ala Leu
                                 25
             20
Ile Asp Lys Phe Asp Ala Asn Pro Tyr Lys Thr Ile Phe Gly Glu Arg
                             40
         35
Lys
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<213> Helicobacter pylori
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                                                                   48
Asn Phe Asn Ser Ala Asn Ile Thr Thr Ser Leu Asn Asn Ser Ser Ile
                                     10
                 -5
gtg ttt aag ggg gcg gtc tct tta gga ggg cag ttt aat tta agc aat
Val Phe Lys Gly Ala Val Ser Leu Gly Gly Gln Phe Asn Leu Ser Asn
                                 25
            20
aac tot tot tta gat tto caa ggo tot ago got ato acc tot aac acg
Asn Ser Ser Leu Asp Phe Gln Gly Ser Ser Ala Ile Thr Ser Asn Thr
                                                 45
                             40
gcg ttt aat ttc tat gat aac gct ttt tct caa agc ccc atc act ttc
Ala Phe Asn Phe Tyr Asp Asn Ala Phe Ser Gln Ser Pro Ile Thr Phe
                        55
cat caa gcc ctt gac att aaa gcg ccc tta agt ttg gga ggc aac ctt
                                                                   240
His Gln Ala Leu Asp Ile Lys Ala Pro Leu Ser Leu Gly Gly Asn Leu
                                         75
tta aac cct aac aac age agc gtg ctg gat tta aaa aac agc cag ctt
                                                                   288
Leu Asn Pro Asn Asn Ser Ser Val Leu Asp Leu Lys Asn Ser Gln Leu
                                     90
gtt ttt ggc gat caa ggg agt ttg aat atc gct aac att gat tta cta
Val Phe Gly Asp Gln Gly Ser Leu Asn Ile Ala Asn Ile Asp Leu Leu
                                105
            100
ago gat cta aat gat aat aaa aat ogt gtg tat aac atc att caa gog
Ser Asp Leu Asn Asp Asn Lys Asn Arg Val Tyr Asn Ile Ile Gln Ala
                            120
gac atg aat agt aat tgg tat gag cgt atc agc ttc ttt ggc atg cac
Asp Met Asn Ser Asn Trp Tyr Glu Arg Ile Ser Phe Phe Gly Met His
                        135
    130
                                                                   455
atc aat gac ggg att tat gat gc
Ile Asn Asp Gly Ile Tyr Asp
145
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Asn Phe Asn Ser Ala Asn Ile Thr Thr Ser Leu Asn Asn Ser Ser Ile
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Val Phe Lys Gly Ala Val Ser Leu Gly Gly Gln Phe Asn Leu Ser Asn
Asn Ser Ser Leu Asp Phe Gln Gly Ser Ser Ala Ile Thr Ser Asn Thr
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Ala Phe Asn Phe Tyr Asp Asn Ala Phe Ser Gln Ser Pro Ile Thr Phe
                         55
His Gln Ala Leu Asp Ile Lys Ala Pro Leu Ser Leu Gly Gly Asn Leu
                                         75
Leu Asn Pro Asn Asn Ser Ser Val Leu Asp Leu Lys Asn Ser Gln Leu
                                     90
                 85
Val Phe Gly Asp Gln Gly Ser Leu Asn Ile Ala Asn Ile Asp Leu Leu
                                105
            100
Ser Asp Leu Asn Asp Asn Lys Asn Arg Val Tyr Asn Ile Ile Gln Ala
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                            120
Asp Met Asn Ser Asn Trp Tyr Glu Arg Ile Ser Phe Phe Gly Met His
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Ile Asn Asp Gly Ile Tyr Asp
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Asp Phe Ser Phe Asn Ala Gln Gly Asn Val Phe Val Gln Asn Ser Thr
                  5
                                     10
tto tot aac goo aat gga ggo acg etc tot tit aac goa gga aat tog
                                                                   96
Phe Ser Asn Ala Asn Gly Gly Thr Leu Ser Phe Asn Ala Gly Asn Ser
                                 25
             20
ctc att ttt gcc gga aac aat cat att gca ttc act aac cac gct gga
                                                                   144
Leu Ile Phe Ala Gly Asn Asn His Ile Ala Phe Thr Asn His Ala Gly
                             40
act ctt caa tta ttg tcc gat caa gtt tct aac att aac atc acc acg
                                                                   192
Thr Leu Gln Leu Leu Ser Asp Gln Val Ser Asn Ile Asn Ile Thr Thr
                                             60
                         55
ctt aac gct agc aac ggc ctt aag att aac gcc gct aat aac aat gtt
                                                                   240
Leu Asn Ala Ser Asn Gly Leu Lys Ile Asn Ala Ala Asn Asn Asn Val
                                         75
                     70
 65
tct gtg tct caa ggc aat ctg ttt gtc agc gct agc tgc gcg caa caa
                                                                   288
Ser Val Ser Gln Gly Asn Leu Phe Val Ser Ala Ser Cys Ala Gln Gln
                                     90
                 85
age gat cca act aca get aat att gea aac eet tge geg ett age
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Ser Asp Pro Thr Thr Ala Asn Ile Ala Asn Pro Cys Ala Leu Ser
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Asp Phe Ser Phe Asn Ala Gln Gly Asn Val Phe Val Gln Asn Ser Thr
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Phe Ser Asn Ala Asn Gly Gly Thr Leu Ser Phe Asn Ala Gly Asn Ser
                                 25
Leu Ile Phe Ala Gly Asn Asn His Ile Ala Phe Thr Asn His Ala Gly
Thr Leu Gln Leu Leu Ser Asp Gln Val Ser Asn Ile Asn Ile Thr Thr
Leu Asn Ala Ser Asn Gly Leu Lys Ile Asn Ala Ala Asn Asn Asn Val
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                                         75
Ser Val Ser Gln Gly Asn Leu Phe Val Ser Ala Ser Cys Ala Gln Gln
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Leu Arg Leu Gly Gln Phe Asn Gly Asn Ser Phe Thr Ser Tyr Lys Asp
                                     10
                  5
age get gat ege ace acg aga gtg gat tte aac get aaa aat ate tta
                                                                   96
Ser Ala Asp Arg Thr Thr Arg Val Asp Phe Asn Ala Lys Asn Ile Leu
             20
att gat aat ttt tta gaa atc aat aat cgt gtg ggt tct gga gcc ggg
Ile Asp Asn Phe Leu Glu Ile Asn Asn Arg Val Gly Ser Gly Ala Gly
         35
agg aaa gcc agc tct acg gtt tta act ttg caa gct tca gaa ggg att
                                                                   192
Arg Lys Ala Ser Ser Thr Val Leu Thr Leu Gln Ala Ser Glu Gly Ile
                         55
act age agt aaa aat geg gaa att tet ett tat gat gge gee aeg ete
                                                                   240
Thr Ser Ser Lys Asn Ala Glu Ile Ser Leu Tyr Asp Gly Ala Thr Leu
                                         75
                     70
aat ttg gct tca aac agc gtt aaa tta atg ggt aat gtg tgg atg ggc
                                                                   288
Asn Leu Ala Ser Asn Ser Val Lys Leu Met Gly Asn Val Trp Met Gly
                                     90
cqt ttg caa tat gtg gga gcg tat ttg gcc cct tca tac agc acg ata
                                                                   336
Arg Leu Gln Tyr Val Gly Ala Tyr Leu Ala Pro Ser Tyr Ser Thr Ile
                                105
            100
                                                                   384
aac act tca aaa gtg aca ggg gaa gtg aat ttt aac cat ctc act gtg
Asn Thr Ser Lys Val Thr Gly Glu Val Asn Phe Asn His Leu Thr Val
                            120
                                                125
        115
ggc gat cac aac gcc gct caa gca ggc att atc gct agt aac aag act
                                                                   432
Gly Asp His Asn Ala Ala Gln Ala Gly Ile Ile Ala Ser Asn Lys Thr
                                            140
   130
                        135
cat att ggc aca ctg gat ttg tgg caa agc gcg gga cta aac att atc
                                                                   480
His Ile Gly Thr Leu Asp Leu Trp Gln Ser Ala Gly Leu Asn Ile Ile
                    150
                                        155
gcc cct cca gaa ggc ggt tat aag gat aaa cct aag gat aaa cct agt
                                                                   528
Ala Pro Pro Glu Gly Gly Tyr Lys Asp Lys Pro Lys Asp Lys Pro Ser
                                    170
               165
aac acc acg caa aat aat gct aac aac aac caa caa aac agc gct caa
Asn Thr Thr Gln Asn Asn Ala Asn Asn Asn Gln Gln Asn Ser Ala Gln
                                185
            180
aac aat agt aac act cag gtt att aac cca ccc aat agc gcg caa aaa
Asn Asn Ser Asn Thr Gln Val Ile Asn Pro Pro Asn Ser Ala Gln Lys
                            200
                                                205
        195
aca gaa att caa ccc acg caa gtc att gat ggg cct ttt gct ggt ggc
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Thr Glu Ile Gln Pro Thr Gln Val Ile Asp Gly Pro Phe Ala Gly Gly
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                                            220
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Leu Arg Leu Gly Gln Phe Asn Gly Asn Ser Phe Thr Ser Tyr Lys Asp
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Ser Ala Asp Arg Thr Thr Arg Val Asp Phe Asn Ala Lys Asn Ile Leu
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30
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Ile Asp Asn Phe Leu Glu Ile Asn Asn Arg Val Gly Ser Gly Ala Gly
Arg Lys Ala Ser Ser Thr Val Leu Thr Leu Gln Ala Ser Glu Gly Ile
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Thr Ser Ser Lys Asn Ala Glu Ile Ser Leu Tyr Asp Gly Ala Thr Leu
Asn Leu Ala Ser Asn Ser Val Lys Leu Met Gly Asn Val Trp Met Gly
                                     90
                 85
Arg Leu Gln Tyr Val Gly Ala Tyr Leu Ala Pro Ser Tyr Ser Thr Ile
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                                105
            100
Asn Thr Ser Lys Val Thr Gly Glu Val Asn Phe Asn His Leu Thr Val
                                                125
                            120
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Gly Asp His Asn Ala Ala Gln Ala Gly Ile Ile Ala Ser Asn Lys Thr
                                            140
                        135
His Ile Gly Thr Leu Asp Leu Trp Gln Ser Ala Gly Leu Asn Ile Ile
                                        155
                   150
Ala Pro Pro Glu Gly Gly Tyr Lys Asp Lys Pro Lys Asp Lys Pro Ser
                                                         175
                                    170
                165
Asn Thr Thr Gln Asn Asn Ala Asn Asn Asn Gln Gln Asn Ser Ala Gln
                                185
            180
Asn Asn Ser Asn Thr Gln Val Ile Asn Pro Pro Asn Ser Ala Gln Lys
                                                205
                            200
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Thr Glu Ile Gln Pro Thr Gln Val Ile Asp Gly Pro Phe Ala Gly Gly
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              - 5
  1
aat ggc tat gtt ttt gtc aat aac agc tct ttt agc aac gct aca gga
                                                                   96
Asn Gly Tyr Val Phe Val Asn Asn Ser Ser Phe Ser Asn Ala Thr Gly
                                                      30
                                 25
ggc agt ttg aat ttt gtc gcc aac aag tct att att ttt aat ggc gat
Gly Ser Leu Asn Phe Val Ala Asn Lys Ser Ile Ile Phe Asn Gly Asp
                                                  45
                              40
 aat acg att gac ttt agc aag tat cag ggc gca ttg att ttt gct tct
                                                                    192
Asn Thr Ile Asp Phe Ser Lys Tyr Gln Gly Ala Leu Ile Phe Ala Ser
                                              60
                          55
 aat gat gtt tot aat atc aat atc acc acc cta aac gct act aat ggc
                                                                    240
 Asn Asp Val Ser Asn Ile Asn Ile Thr Thr Leu Asn Ala Thr Asn Gly
                                         75
                      70
  65
 tta agc ctt aat gcg ggt ttg aat aac gtg agc gtt caa aaa gg
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 Leu Ser Leu Asn Ala Gly Leu Asn Asn Val Ser Val Gln Lys
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                                      10
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  1
                                 25
              20
 Gly Ser Leu Asn Phe Val Ala Asn Lys Ser Ile Ile Phe Asn Gly Asp
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40
         35
Asn Thr Ile Asp Phe Ser Lys Tyr Gln Gly Ala Leu Ile Phe Ala Ser
                         55
Asn Asp Val Ser Asn Ile Asn Ile Thr Thr Leu Asn Ala Thr Asn Gly
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Leu Ser Leu Asn Ala Gly Leu Asn Asn Val Ser Val Gln Lys
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<221> CDS
<222> (1) . . (498)
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Lys Ile Leu Val Ile Gln Gly Pro Asn Leu Asn Met Leu Gly His Arg
                                     10
gac cca agg ctt tat ggt atg gta acc tta gac caa atc cat gaa atc
Asp Pro Arg Leu Tyr Gly Met Val Thr Leu Asp Gln Ile His Glu Ile
                                 25
atg caa act ttc gtg aaa caa ggc aat tta gat gtg gaa tta gag ttt
Met Gln Thr Phe Val Lys Gln Gly Asn Leu Asp Val Glu Leu Glu Phe
                             40
         35
ttt caa act aat ttt gag ggc gaa atc att gat aaa atc caa gag agc
                                                                   192
Phe Gln Thr Asn Phe Glu Gly Glu Ile Ile Asp Lys Ile Gln Glu Ser
                        55
                                              60
    50
gtg ggc agc gat tat gaa ggg atc atc att aac cct gga gcg ttt tcg
                                                                   240
Val Gly Ser Asp Tyr Glu Gly Ile Ile Ile Asn Pro Gly Ala Phe Ser
                     70
cac act tot att gog att goa gat gog atc atg ota gog ggc aaa coc
                                                                   288
His Thr Ser Ile Ala Ile Ala Asp Ala Ile Met Leu Ala Gly Lys Pro
                                                          95
                 85
                                     90
gtt att gaa gtg cat ctc act aac att caa gcc aga gag gaa ttc agg
                                                                   336
Val Ile Glu Val His Leu Thr Asn Ile Gln Ala Arg Glu Glu Phe Arg
                                105
aaa aat tot tac act gga gcg gct tgt gga ggc gtg atc atg gga ttt
                                                                   384
Lys Asn Ser Tyr Thr Gly Ala Ala Cys Gly Gly Val Ile Met Gly Phe
                            120
        115
ggc ccg ctt ggc tac aac atg gct tta atg gcg atg gtc aat att tta
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Gly Pro Leu Gly Tyr Asn Met Ala Leu Met Ala Met Val Asn Ile Leu
                        135
qcc gaa atg aaa gcg ttc caa gaa gcc caa aaa aac aac cct aat aac
                                                                   480
Ala Glu Met Lys Ala Phe Gln Glu Ala Gln Lys Asn Asn Pro Asn Asn
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145
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ccc att aac aat caa aaa
Pro Ile Asn Asn Gln Lys
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<213> Helicobacter pylori
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Lys Ile Leu Val Ile Gln Gly Pro Asn Leu Asn Met Leu Gly His Arg
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Asp Pro Arg Leu Tyr Gly Met Val Thr Leu Asp Gln Ile His Glu Ile
                                 25
Met Gln Thr Phe Val Lys Gln Gly Asn Leu Asp Val Glu Leu Glu Phe
                                                  45
                             40
Phe Gln Thr Asn Phe Glu Gly Glu Ile Ile Asp Lys Ile Gln Glu Ser
                         55
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Val Gly Ser Asp Tyr Glu Gly Ile Ile Asn Pro Gly Ala Phe Ser
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His Thr Ser Ile Ala Ile Ala Asp Ala Ile Met Leu Ala Gly Lys Pro
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                 85
Val Ile Glu Val His Leu Thr Asn Ile Gln Ala Arg Glu Glu Phe Arg
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            100
Lys Asn Ser Tyr Thr Gly Ala Ala Cys Gly Gly Val Ile Met Gly Phe
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                            120
Gly Pro Leu Gly Tyr Asn Met Ala Leu Met Ala Met Val Asn Ile Leu
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Ala Glu Met Lys Ala Phe Gln Glu Ala Gln Lys Asn Asn Pro Asn Asn
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Pro Ile Asn Asn Gln Lys
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 Gln Ser Leu Ile Thr Ile Ile Asn Arg Leu Met Gln Lys Gln Asp Gln
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 cga cta tca tcg ctc aag gca caa aaa
 Arg Leu Ser Ser Leu Lys Ala Gln Lys
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 Phe Asn Asn Ser Ala Ser Phe Asn Phe Asn Asn Ser Asn Ala Thr Thr
                                       10
                   5
   1 .
  tog tit gig ggg gat tic act aac got aat toa aat tig caa ato goo
  Ser Phe Val Gly Asp Phe Thr Asn Ala Asn Ser Asn Leu Gln Ile Ala
                                                       30
                                   25
              20
  ggg aac gct gtt ttt ggg aac tct act aat ggc tct caa aat acc gct
  Gly Asn Ala Val Phe Gly Asn Ser Thr Asn Gly Ser Gln Asn Thr Ala
                                                   45
                               40
  aat ttt aat aat acc ggc tct gtt aat att tca ggg aat gca acc ttt
           35
                                                                     192
  Asn Phe Asn Asn Thr Gly Ser Val Asn Ile Ser Gly Asn Ala Thr Phe
                                               60
                           55
  gat aat gtg gtg ttt aat ggc cct acg aac acg agc gtg aaa ggg cag
  Asp Asn Val Val Phe Asn Gly Pro Thr Asn Thr Ser Val Lys Gly Gln
                                           75
                       70
  gtt act tta aat aac atc act tta aaa aac ctg aac gcc cct ttg tct
   65
                                                                     288
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	Thr			85					90					95		
+++	ggc	gat	aaa	aca	att	act	ttt	aac	act	cat	tcq	qtq	att	aat	att	336
DL -	Gly	7	999	mb-	Tlo	Thr	Pho	Aen	Δla	Hie	Ser	Val	Ile	Asn	Ile	
Pne	GIÀ	Asp		Int	116	1111	1110		7120				110			
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Δla	Glu	Ser	Tle	Thr	Asn	GIV	Asn	Pro	Ile	Thr	Leu	Val	Ser	Ser	Ser	
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Lvs	Glu	Ile	Glu	Tyr	Asn	Asn	Ala	Phe	Ser	Lys	Asn	Leu	Trp	Gln	Leu	
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WIG	GTĀ	Mon	GLY		- 7 -	1101			170					175		
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Tyr	Asn	Phe	Gln	Glu	Val	Phe	Ser	Gln	Asn	Ser	Ile	Ser	Ile	Arg	Arg	
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**-	ggc	-++	220	2+0	ata	+++	nat	tat	ata	gat	atα	gaa	aaa	tca	gat	624
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Hie	Leu	Tur	Tyr	Gln	Asn	Ala	Leu	Glv	Phe	Met	Thr	Tyr	Met	Pro	Asn	
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Thr Ser Leu Asn Asn Ser Ser Ile Val Phe Lys Gly Ala Val Ser Leu
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Ser Ser Ala Ile Thr Ser Asn Thr Ala Phe Asn Phe Tyr Asp Asn Ala
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Phe Ser Gln Ser Pro Ile Thr Phe His Gln Ala Leu Asp Ile Lys Ala
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Pro Leu Ser Leu Gly Gly Asn Leu Leu Asn Pro Asn Asn Ser Ser Val
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Leu Asp Leu Lys Asn Ser Gln Leu Val Phe Gly Asp Gln Gly Ser Leu
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                             120
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Asn Ile Ala Asn Ile Asp Leu Leu Ser Asp Leu Asn Asp Asn Lys Asn
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Arg Val Tyr Asn Ile Ile Gln Ala Asp Met Asn Ser Asn Trp Tyr Glu
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Arg Ile Ser Phe Phe Gly Met His Ile Asn Asp Gly Ile Tyr Asp Ala
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               · 165
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 Lys Asn Gln Thr Tyr Ser Phe Thr Asn Pro Leu Asn Asn Ala Leu Lys
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 Ile Thr Glu Ser Phe Lys Asp Asn Gln Leu Ser Val Thr Leu Ser Gln
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 Ile Pro Gly Ile Lys Asn Thr Leu Tyr Asn Ile Gly Ser Glu Ile Phe
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Ser Ser Ala Ile Thr Ser Asn Thr Ala Phe Asn Phe Tyr Asp Asn Ala
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Leu Asp Leu Lys Asn Ser Gln Leu Val Phe Gly Asp Gln Gly Ser Leu
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Arg Ile Ser Phe Phe Gly Met His Ile Asn Asp Gly Ile Tyr Asp Ala
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Lys Asn Gln Thr Tyr Ser Phe Thr Asn Pro Leu Asn Asn Ala Leu Lys
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Ile Pro Gly Ile Lys Asn Thr Leu Tyr Asn Ile Gly Ser Glu Ile Phe
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Leu Arg Ala Lys Asn Ile His Ile Asn Phe Gln Gly Val Ser Thr Phe
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Ser Leu Leu Asn Phe Asn Gly Asn Ser Val Phe Asn Ala Pro Val Ser
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Phe Tyr Ala Asn His Ser Gln Ile Ser Phe Thr Lys Leu Ala Thr Phe
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Gln	Ser	Val 115	Leu	Leu	Asn	Gly	Ala 120	Leu	Asn	Leu	Leu	Gly 125	Asn	Gly	Ser	
	+	cta	aca	atc	aac	act	aaa	ggg	aat	ttt	agt	ttt	ggg	tct	aaa	432
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		Val		165					170					1/2		
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Gly	Thr	Tyr	Asn	Ala	Gln	Asn 295	Gln	Pro	Leu	GIN	300	Leu	HIS	TTe	ıyı	
aat	C3.C	act	atc	act	aag	caa	gat	ttg	aac	atg	atc	gcc	agt	ttg	ggt	960
Asn	Gln	Ala	Ile	Thr	Lys	Gln	Asp	Leu	Asn	Met	TTE	Ala	Ser	Leu	GTA	
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T.vs	Glu	Phe	Leu	Pro	Lys	Ile	Ála	Asn								
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Lys	Gln		20 Ser	Thr	Met	Asn	Leu		Glu	Ser	Ser	Gln 45	Ala		Phe	
Asn	Ala	35 Leu	Lys	Val	Glu		40 Glu	Thr	Asn	Phe	Asn	Leu		Asn	Ser	
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Phe	Tyr	Ala	Asn	HIS	ser	eTu	TTE	Set	FUE	# 11T	пyэ	T-C (T	****		Phe	

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Thr				165					170	• •				Leu 175		
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		195					200				Ī	205		Phe		
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			260					265					270	Thr		
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_	290					295					300			Ile		
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_	Glu		Leu	32 <u>5</u>	гàз	IIe	ATA	ASII								
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1				5					10					12		96
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Ala Asp Ile Val Met Cys Asp Asn Leu Ser Val Leu Glu Thr Lys Glu
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Ile Ala Ala Tyr Arg Asp Ala His Tyr Pro Phe Val Leu Leu Glu Ala
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acc agg caa ggc aaa gac ata gcc ata cgc ctt aaa gac gct ccc aag
                                                                    144
Thr Arg Gln Gly Lys Asp Ile Ala Ile Arg Leu Lys Asp Ala Pro Lys
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ttg ggg ctc tct caa ggg gat att tta ttt aaa gaa gag aag gaa att
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Leu Gly Leu Ser Gln Gly Asp Ile Leu Phe Lys Glu Glu Lys Glu Ile
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age gtg gca gaa gta gcg aaa ata tgc tat gaa ata gga aac cgc cat
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Ser Val Ala Glu Val Ala Lys Ile Cys Tyr Glu Ile Gly Asn Arg His
gcg gct tta tac tat ggc gag tct caa ttt gaa ttt aaa aca cca ttt
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Ala Ala Leu Tyr Tyr Gly Glu Ser Gln Phe Glu Phe Lys Thr Pro Phe
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gaa aag ccc acg cta gcg tta tta gaa aag cta ggg gtt caa aat cgt
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Glu Lys Pro Thr Leu Ala Leu Leu Glu Lys Leu Gly Val Gln Asn Arg
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         115
 gtt tta agt tca aaa ttg gat tcc aaa gaa cgc tta acc gtg agc atg
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Glu Lys Pro Thr Leu Ala Leu Leu Glu Lys Leu Gly Val Gln Asn Arg
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Asp Leu Val Lys Glu Gln Lys Asp Leu Val Lys Thr Gln Lys Asp Phe
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 Pro Lys His Leu Pro Asn Ser Lys Gln Pro Arg Ser Gln Arg Gly Ser
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Se	r Lei	ı Lei	ı Phe	e Val 245	L Gl	l Lys	s Ile	e Phe	250	a Asp)	y Val	L Ası	n Lys	s Glu 255	ı Ile	

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Leu Asp Thr Lys Val Val Pro Lys Gly Ser Val Asp Lys Leu Phe Ile
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Leu	PLO	Tyr	ASP	Arg	GIU	M311	Ser	MIG	LCG	2,30		• • • • • • • • • • • • • • • • • • • •	-,-		- 4	
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gcc	aaa	cag	cat	gcg	τττ	ttg	aac	gcg	- LLa	yaa	cyc	909	2	7	*1.	-
Δla	T.VS	Gln	His	Ala	Phe	Leu	Asn	Álá	Leu	Glu	Cys	GIU	Ser	Leu	TTE	
	-,-			165					170					175		
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-	m	WF	D	LAN	Hic	Δla	ום, ו	Leu	Len	Asp	Leu	Leu	Asp	Phe	Pro	
PIO	ryr	THE	PTO	µ€u	1173	27.0	يان نا				220					
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att	grà		acy	age	909	3	Dha	Com	60=	Lou	Dro	T.A.II	Δla	Ser	Asp	
Ile	Val	Phe	Thr	Ser	ATa	ASI	rne	Ser	Ser	neu	FIU	Tien	niu		240	
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Leu 305	Ala	Leu	Gly	Ala	Gln 310	Gln	Lys	Gly	His	Phe 315	Ser	Leu	Leu	Asp	Ser 320	
000	act	tcc	att	ctt		ctc	tca	cct	ttt	tat	aga	gat	ttg	agc	gtt	1008
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tta	gaa	aat	gaa	aaa	cac	רננ	daa	yaa Cl	mb-	Tou	nac nac	Pho	Dha	Leu	Tue	1000
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Glv	Asp	Leu	Ğlu	Ara	Ile	Glu	Glu	Thr	Ala	Arg	Phe	Glu	Glu	Phe	Trp	
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Tan	Leu	799 Clu	610	Gln	Luc	Ala	Tle	Lvs	Glu	Pro	Ara	Ara	Leu	Val	Leu	
Leu		GLY	Gry	GIII	цуз	455		-,-			460	5			•	
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gaa	Ile	gct	T	aaa	ude	Cla	Ton	700	Tue	Lou	Len	Lve	Ara	Val	Gln	
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Cys	Asn	GIN	Leu	Leu	cys		GIU	reu	WTQ	nys	TIG.	TEG	vrā	GIĀ	AC U	
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_			100					105					110	Ile	•	
_		115					120					125		Leu		
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	Arg	Pro	Leu	Lys	Pro 150	Phe	Ala	Leu	мет	155	ьys	Asp	rea	Asn ·	160	
145 Ala	Lys	Gln	His	Ala 165	Phe	Leu	Asn	Ala	Leu 170		Cys	Glu	Ser	Leu 175	Ile	
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Gly Ser Gly Ala Tyr Glu Asn Lys Ile Tyr Gly Ala Glu Cys Phe Val
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                                425
            420
Gly Asp Leu Glu Arg Ile Glu Glu Thr Ala Arg Phe Glu Glu Phe Trp
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Leu Leu Gly Gly Gln Lys Ala Ile Lys Glu Pro Arg Arg Leu Val Leu
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Glu Ile Ala Leu Lys His Gln Leu Asn Lys Leu Leu Lys Arg Val Gln
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Lys His Phe Lys Glu Asp Glu Leu Glu Ile Phe Gln Gln Met His Asp
                                     490
                485
Lys Lys Ile Gln Ser Ile Ala Thr Asn Ser Ile Gly Arg Leu Phe Asp
                                 505
            500
Ile Val Ala Phe Ser Leu Asp Leu Thr Gly Thr Ile Ser Phe Glu Ala
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Glu Ser Gly Gln Val Leu Glu Asn Leu Ala Leu Gln Ser Asp Glu Ile
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                         535
Ala Phe Tyr Pro Phe Glu Ile Lys Asn Ser Val Val Cys Leu Lys Glu
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                                         555
                    550
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Phe Tyr Gln Ala Phe Glu Lys Asp Leu Gly Val Leu Glu Pro Glu Arg
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Ile Ala Lys Lys Phe Phe Asn Ser Leu Val Glu Ile Ile Thr Ala Leu
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                                 585
            580
Ile Val Pro Phe Lys Glu His Val Val Cys Ser Gly Gly Val Phe
                                                 605
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Cys Asn Gln Leu Leu Cys Glu Gln Leu Ala Lys Arg Leu Arg Gly Leu
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                         615
Lys Arg Gln Tyr Phe Phe His Lys His Phe Pro Pro Asn Asp Ser Ser
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                                                                    96
 Val Arg Lys Phe Tyr Arg His Lys Lys Trp Val Asp Ala Asp Val Trp
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 caa atg gaa aaa tta ctg cct gga aat gaa gtc ata gga cct gcg atc
 Gln Met Glu Lys Leu Leu Pro Gly Asn Glu Val Ile Gly Pro Ala Ile
                                                  45
                              40
 gtg gaa toa gat gog acc act tto gtg ata occ aaa ggo ttt gog aca
 Val Glu Ser Asp Ala Thr Thr Phe Val Ile Pro Lys Gly Phe Ala Thr
                          55
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Val Glu Ser Asp Ala Thr Thr Phe Val Ile Pro Lys Gly Phe Ala Thr
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Arg Leu Asp Lys His Arg Leu Phe His Leu Lys Glu Ile Lys
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Leu Phe Lys Phe Asn Arg Leu His Thr Lys Ile Ser Ile Leu Gln Asp
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             20
gag aaa ccc atc tat tat gac aac acg att tta gat ccc aaa acc acc
Glu Lys Pro Ile Tyr Tyr Asp Asn Thr Ile Leu Asp Pro Lys Thr Thr
                             40
gac tta aat aac atg tgc atg ttt gat ggc tat acg cat tat ttg aat
                                                                   192
Asp Leu Asn Asn Met Cys Met Phe Asp Gly Tyr Thr His Tyr Leu Asn
                         55
ttg gtg ctt gtc aat tgc ccc ata gag ctc tct ggt gtg cga gaa tgc
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att gaa gaa agc gaa ggg gtg gat ggg gca gtg agt gaa acc gct agt
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Ile Glu Glu Ser Glu Gly Val Asp Gly Ala Val Ser Glu Thr Ala Ser
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tot cat tta tgc gtg aaa gct tta gcg aaa ggc tca gaa ccc tta ttg
Ser His Leu Cys Val Lys Ala Leu Ala Lys Gly Ser Glu Pro Leu Leu
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            100
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Ser His Leu Cys Val Lys Ala Leu Ala Lys Gly Ser Glu Pro Leu Leu
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aat ggt gag aac ttg agc gct atc aaa aaa gat tta cct cta tta aca
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Asn Gly Glu Asn Leu Ser Ala Ile Lys Lys Asp Leu Pro Leu Leu Thr
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 Met Asp Tyr Gln Lys Gln Asp Ile Ile Lys Met Phe Tyr Pro Leu Val
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 Lys Val Arg Tyr Glu Asn Asp Lys Tyr Leu Ile Pro Phe Ala Ser Leu
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 65
 gac gcc aat caa aga atg gaa ttt gac ttg aaa gat cct caa ggc aag
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 Asp Ala Asn Gln Arg Met Glu Phe Asp Leu Lys Asp Pro Gln Gly Lys
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	0> 7									•						
	1> 2															
	2> P 3> H		obac	ter	ovlo	ri										
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Thr	Ser	Leu		- 5					10					Asp 15		
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Lys Ile Asp Ser Lys Asn Ile Tyr Ile Leu Gly Glu Ser Lys Glu Glu
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46	5				470	) . ~~~	, ,,,+	tat	tet			a dad	cti	: tto	g gaa	1488
tte	g aca	ato	cat	gcg	CTT	. yaç	, aal 1 Aer	Cvs	Ser	Ast	Gli	ı Glı	Lei	ı Lei	Glu	
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Tu-	r Ala	Lvs	Ası	o Tre	Ser	Lys	Gĺy	v Val	Lys	Mét	: Ala	ıle	ELL	ya.	l Phe	
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Gln Phe Leu Ser Cys Gly Leu Leu Glu Ile Lys Gly Lys Asn Gly Ala
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Ser Met Glu Phe Cys Leu Pro Lys Val Tyr Pro Phe Pro Pro Lys Ser
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Leu Tyr Ile Glu His Glu Lys Asp Gly Gln Phe Leu Arg Glu Met Leu
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Met Arg Leu Ser Ser Ala Pro Leu Val Gln Leu Glu Val Ile Leu
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Val Asp Ala Leu Ser Leu Gly Gly Ile Phe Asn Leu Ala Arg Arg Leu
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Leu His Lys Asp Asn Asp Phe Ile Tyr Gln Gln Arg Ile Leu Thr Glu
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Ser Lys Glu Ile Glu Glu Ala Leu Lys His Leu Tyr Glu Tyr Leu Lys
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Val Asn Leu Gln Glu Lys Leu Ala Gly Tyr Lys Asp Phe Ala His Tyr
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Asn Glu Glu Lys Lys Asp Arg Leu Pro Leu Lys Ala Leu Phe Leu Ser
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Gly Val Asp Ala Leu Ser Gln Asn Ala Leu Tyr Tyr Leu Glu Lys Ile
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Met Arg Phe Gly Ser Lys Asn Gly Val Leu Ser Phe Val Asn Leu Glu
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Ser Glu Lys Asn Asn Lys Ser Thr Glu Asp Leu Lys Arg Tyr Ala Glu
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               245
Cys Phe Lys Asp Arg Thr Ser Phe Glu Arg Leu Lys Tyr Leu Asn Ile
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            260
Glu Val Ile Asn Asp His Gly Ile Gln Ser Lys His Met Lys Asp Phe
                                               285
                            280
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Ala Asp Lys Ile Lys Ala Tyr Tyr Glu Lys Lys Ala Val Lys Arg
                                            300
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 Glu Leu Lys Asp Leu Gln Lys Asp Glu Lys Phe Trp Thr Glu Ser Ser
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age gag tte atg aaa gee tat ace gea ttg eta aaa aaa caa gae ega
                                                                   96
Ser Glu Phe Met Lys Ala Tyr Thr Ala Leu Leu Lys Lys Gln Asp Arg
                                                      30
                                 25
tac gtc tat tta ttg agg tat ctc ccc tct agg tat tgg gcc agc att
Tyr Val Tyr Leu Leu Arg Tyr Leu Pro Ser Arg Tyr Trp Ala Ser Ile
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tta acg act gcc ctt tat gtc aaa tac cct gat ttt gac gct ttg aaa
                                                                   192
Leu Thr Thr Ala Leu Tyr Val Lys Tyr Pro Asp Phe Asp Ala Leu Lys
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aag ctt ttg gtg tct tat tat tac caa act tgg att gca gga ggc acg
Lys Leu Leu Val Ser Tyr Tyr Tyr Gln Thr Trp Ile Ala Gly Gly Thr
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                     70
ate acg ege ate aag caa ace agt ate aac att ate aaa aac gtt aaa
                                                                   288
Ile Thr Arg Ile Lys Gln Thr Ser Ile Asn Ile Ile Lys Asn Val Lys
                                     90
                 85
age aat aag age gtt gaa ace ate aaa gag ett ata ttg aat age ate
Ser Asn Lys Ser Val Glu Thr Ile Lys Glu Leu Ile Leu Asn Ser Ile
                                105
gae tet tat aac ace ttt gat caa tac etc tat aac tta tgg gat age
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Asp Ser Tyr Asn Thr Phe Asp Gln Tyr Leu Tyr Asn Leu Trp Asp Ser
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                            120
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tet tet gtt tat cat age aaa tgg gtg egt eet gte tta gee eta get
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Ser Ser Val Tyr His Ser Lys Trp Val Arg Pro Val Leu Ala Leu Ala
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aat tat ttc atg gca gat gaa gag aaa ccc cat ttt atc gct atg gat
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Asn Tyr Phe Met Ala Asp Glu Glu Lys Pro His Phe Ile Ala Met Asp
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                    150
gcc gaa acc caa gtg gag cat att ttg cca caa acg ccc aaa aga ggc
Ala Glu Thr Gln Val Glu His Ile Leu Pro Gln Thr Pro Lys Arg Gly
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                165
agt caa tgg aac gcg gat ttt gac aaa gaa aaa aga gaa gaa tgg gta
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Ser Gln Trp Asn Ala Asp Phe Asp Lys Glu Lys Arg Glu Glu Trp Val
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Asn Asn Ile Ala Asn Leu Thr Leu Leu Lys Arg Lys Lys Asn Ala His
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Ala Leu Asn Gly Asp Phe Asp Glu Lys Arg Lys Ile Tyr Gly Gly Lys
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gac acg agc aaa gtg att agc tgt tat gac atc act aaa gaa ttg tat
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Asp Thr Ser Lys Val Ile Ser Cys Tyr Asp Ile Thr Lys Glu Leu Tyr
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Ser Asn Tyr Arg Lys Trp Asn Glu Lys Ser Leu Gln Glu Arg Tyr Lys
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                                     250
                245
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Asp Asp Phe Glu Asp Asp Phe Asp Leu Glu
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Ser Asn Lys Ser Val Glu Thr Ile Lys Glu Leu Ile Leu Asn Ser Ile
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Asp Ser Tyr Asn Thr Phe Asp Gln Tyr Leu Tyr Asn Leu Trp Asp Ser
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Ser Ser Val Tyr His Ser Lys Trp Val Arg Pro Val Leu Ala Leu Ala
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Asn Tyr Phe Met Ala Asp Glu Glu Lys Pro His Phe Ile Ala Met Asp
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Ala Glu Thr Gln Val Glu His Ile Leu Pro Gln Thr Pro Lys Arg Gly
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Ser Gln Trp Asn Ala Asp Phe Asp Lys Glu Lys Arg Glu Glu Trp Val
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Asn Asn Ile Ala Asn Leu Thr Leu Leu Lys Arg Lys Lys Asn Ala His
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Ala Leu Asn Gly Asp Phe Asp Glu Lys Arg Lys Ile Tyr Gly Gly Lys
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Asp Thr Ser Lys Val Ile Ser Cys Tyr Asp Ile Thr Lys Glu Leu Tyr
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 Ser Asn Tyr Arg Lys Trp Asn Glu Lys Ser Leu Gln Glu Arg Tyr Lys
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 Gln Asn Pro Tyr Pro Glu Glu Val Arg Phe Asn Glu Leu Arg Leu Ala
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		35					40									100
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Leu	Gly	Asn	Val	Ala	Leu	Val	Arg	Glu 105	Glu	Leu	Leu	Leu	Gly 110	Val		
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	3> He		bact	ter r	vlo	ci										
1101	15 88	2														
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Gln	Asn	Pro	Tyr 20	Pro	Glu	Glu	Val	Arg 25	Phe	Asn	Glu	Leu	Arg 30	Leu	Ala	
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Lys	Gly	Phe	Ile	Pro	Lys	Gly	Tyr	Leu	Trp	His	Phe	Asp	Ala	Asn	Val	
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	0> 89															
	1> 10															
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Leu	Val	Ser	Ser	Ser	GIU	Tyr	. ALA	ьys	10	Dea	110			15	-1-	
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Ser	Asp	Ser	Pro	Val	Arg	Met 55	Tyr	Leu	Arg	GIU	мет 60	GIY	Asp	TTE	гÀЗ	
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CLL	t cid	ayc	Luc	ya. Den	Glii	Glu	Ile	Glu	Leu	Ser	Lys	Gln	Ile	Arg	Leu	
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ggt	gaa	yac	71~	Tin	T.e.	Aen	Ala	Ile	Cvs	Ser	Val	Pro	Tyr	Leu	Ile	
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vai	гÃ2		пеп	1110	9		120		•	•	•	125				
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Ser	Leu	Thr	Leu	Ala	Tyr	Lys	Arg	GIN	Inr	Leu	гÀ2	ASP	ALG	rea	TAT	
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Pne			GIU	Буз	Gry	375					380			•	-	
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Ile	. Lys	Gln	ALa	Ile			ATS	116	MIG	voh	GII	, ATG	MIG	, ,,,,,	1le 400	
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- meT	- ALC	uy3						- 4	-			•				

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Pne	GIĀ	515	Deu	ASP	nsp	GIU	520	nop	9			525				
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225 Lew Glu Tyr Lys Leu Pro Leu Phe Asn Asp Thr Leu Ile Ala Asn His 245 Lys Lys Ile Leu Ala Asn Ile Thr Asn Met Thr Lys Glu Asp Ile Ile 256 270 Ala Gln Val Pro Glu Ala Thr Met Val Ser Val Tyr Met Asp Leu Lys 275 Lys Leu Phe Leu Thr Lys Glu Ala Ser Glu Glu Gly Phe Asp Leu Lys 290 295 Pro Asn Lys Leu Lys Glu Ile Leu Glu Gln Ile Lys Arg Gly Lys Leu 305 305 116 Ser Asp Arg Ala Lys Asn Lys Met Ala Lys Ser Asn Leu Arg Leu 325 Val Val Ser Ile Ala Lys Arg Phe Thr Ser Arg Gly Leu Pro Phe Leu 335 Asp Leu Ile Gln Glu Gly Asn Ile Gly Leu Met Lys Ala Val Asp Lys 365 Phe Glu His Glu Lys Gly Phe Lys Phe Ser Thr Tyr Ala Thr Trp Trp 370 375 380 Arg Ile Pro Ile His Met Ile Asp Thr Ile Asn Arg Ile Asn Lys Val 405 Arg Ile Fro Ile His Met Ile Asp Thr Ile Asn Arg Ile Asn Lys Val 405 Arg Ile Fro Ile His Met Ile Asp Thr Ile Asn Arg Ile Asn Lys Val 405 Asp Asp Gly Lys Leu Glu Val Gly Leu Ser Leu Glu Thr Pro Val Gly Asn Val 405 Arg Ile Fro Ile His Met Arg Glu Asp Leu Glu Val 425 Val Ala Glu Glu Val Gly Eeu Ser Leu Glu Thr Pro Val Gly Asn Asp 460 Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Val Ile 465 Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Val Ile 465 Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Ile Val Ser 470 Asp Asp Gly Lys Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Gly Lys Glu Pro Asp Leu Glu Val 465 Asp Asp Gly Lys Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Gly Asn Asp 460 Asp Asp Gly Lys Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Gly Asn Asp 465 Asp Asp Gly Lys Leu Asn Glu Arg Glu Asp Leu Lys Ala Gln Ile Glu Ser 470 Ser Ile Asp His Ile Met Arg Glu Asp Leu Lys Ala Gln Ile Glu Ser 555 Tyr Leu Arg Ile Call Asp Glu Arg Gly Asp Asp Gly Arg Ile Leu Arg Asn 554 Tyr Leu Arg Ile Call Asp Glu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 560 Tyr Leu Arg Ile Call Asp Call Asp Asn Thr Arg Lys Ser Asp Ala Lys Ser Val 110 Asa Call Glu Asp Leu Ala Lys Asn Thr Arg Lys Ser Asp Ala Lys Ser Val 110 Asa Call Glu Asp Leu Tyr His Glu Pre Ser Glu Asp Lys Arg Ser Ile 110 Asa Call Glu Asp Leu Tyr His Glu Pre Ser Glu Asp Lys Arg Ser Ile 110																	
245	225		a,			230						_				240	
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Lys Leu Phe Leu Thr Lys Glu Ala Ser Glu Glu Gly Phe Asp Leu Ala 295			275					280					285				
Pro Asn Lys Leu Lys Glu Ile Leu Glu Gln Ile Lys Arg Gly Lys Leu 305	-	200	Phe				295					300					
The Ser Asp Arg Ala Lys Asn Lys Met Ala Lys Ser Asn Leu Arg Leu 325	205	Asn				310					<b>312</b>					320	
Asp Leu Ile Gln Glu Gly Asn Ile Gly Leu Met Lys Ala Val Asp Lys 355 360  Phe Glu His Glu Lys Gly Phe Lys Phe Ser Thr Tyr Ala Thr Trp Trp 370 375  Ile Lys Gln Ala Ile Ser Arg Ala Ile Ala Asp Gln Ala Arg Thr Ile 400 400 415  Met Arg Lys His Met Ile Asp Thr Ile Asn Arg Ile Asn Lys Val 415  Met Arg Lys His Ile Gln Glu Asn Gly Lys Glu Pro Asp Leu Glu Val 425 430  Val Ala Glu Glu Val Gly Leu Ser Leu Asp Lys Val Lys Asn Val Ile 435  Lys Val Thr Lys Glu Pro Ile Ser Leu Glu Thr Pro Val Gly Asn Asp 450  Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Ile Val Ser 460  Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Ile Val Ser 460  Val Leu Asp Gln Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Met Arg 500  Phe Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Glu Ser 490  Ple Gly Leu Leu Asp Val Thr Arg Glu Arg Val Arg Gln Ile Gly Ser 530  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 540  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 540  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 540  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 540  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 540  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 540  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 550  Tyr Leu Arg Ile 2210 91	Ile				325					330					222		
Signature   Sign				340					345					330			
370  11e Lys Gln Ala 1le Ser Arg Ala 1le Ala Asp Gln Ala Arg Thr Ile Ash Lys Gln Ala 1le Ser Arg Ala 1le Ala Asp Gln Ala Arg Thr Ile Ash Arg Ile Pro Ile His Met Ile Ash Thr Ile Ash Arg Ile Ash Lys Val 405  Met Arg Lys His Ile Gln Glu Ash Gly Lys Glu Pro Asp Leu Glu Val 420  Val Ala Glu Glu Val Gly Leu Ser Leu Asp Lys Val Lys Ash Val Ile Ash Ash Val Ile Ash Arg Val Ile Ash Lys Val Thr Lys Glu Pro Ile Ser Leu Glu Thr Pro Val Gly Ash Asp 450  Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Leu Lys Ash Gln Ile Glu Ser Asp Asp Gly Leu Ash Ash Glu Asp Leu Lys Ash Gln Ile Gly Ser Ile Ash His Ile Met Arg Glu Asp Leu Lys Ala Gln Ile Gly Ser Asp Asp Gly Leu Leu Ash Glu Arg Glu Lys Ala Val Ile Arg Met Arg 500  Phe Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Ile Gly Ser Ser Silo  Phe Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Ile Gly Ser Ser Silo  Phe Gly Leu Ash Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser Ser Silo  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Ash Silo Silo Silo Silo Silo Silo Silo Silo	•		355					360					365				
385 Arg Ile Pro Ile His Met Ile Asp Thr Ile Asn Arg Ile Asn Lys Val 405 Met Arg Lys His Ile Gln Glu Asn Gly Lys Glu Pro Asp Leu Glu Val 420 Val Ala Glu Glu Val Gly Leu Ser Leu Asp Lys Val Lys Asn Val Ile 435 Lys Val Thr Lys Glu Pro Ile Ser Leu Glu Thr Pro Val Gly Asn Asp 450 Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Ile Val Ser 450 Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Ile Val Ser 465 Asp Asp Gly Leu Asn Glu Arg Glu Asp Leu Lys Ala Gln Ile Glu Ser 480 Val Leu Asp Gln Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Met Arg 500 Phe Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Ile Gly 515 Lys Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser Ser 530 Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 545 Tyr Leu Arg Ile <210> <221> CDS <222> (1)(237) <400> 91 aaa cta gtt tta gcc aag aat aca aga aaa tca gcc gct aag agc gtg Lys Leu Val Leu Asp Leu Tyr His Glu Phe Ser Glu Asp Lys Arg Ser Ile Glu Leu Glu Asp Leu Tyr His Glu Phe Ser Glu Asp Lys Arg Ser Ile 20 ttc tat ttt gcc ccc aca aac gcc cac aaa gac atg ctc aaa gcg gtg Phe Tyr Phe Ala Pro Thr Asn Ala His Lys Asp Met Leu Lys Ala Val  450  401  425  430  426  427  428  429  429  425  430  430  431  445  445  445  445  445  445  445		270					375					380					
Met Arg Lys His Ile Gln Glu Asn Gly Lys Glu Pro Asp Leu Glu Val 420  Val Ala Glu Glu Val Gly Leu Ser Leu Asp Lys Val Lys Asn Val Ile 435  Lys Val Thr Lys Glu Pro Ile Ser Leu Glu Thr Pro Val Gly Asn Asp 450  Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Ile Val Ser 465  Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Ile Glu Ser 465  Ser Ile Asp His Ile Met Arg Glu Asp Leu Lys Ala Gln Ile Glu Ser 480  Val Leu Asp Gln Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Met Arg 500  Phe Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Ile Gly 515  Lys Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser 530  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 545  Tyr Leu Arg Ile <210> <11> 211> 237 <121> DNA <1213  Helicobacter pylori <220> <221> CDS <222> (1)(237) <400> 91  aaa cta gtt tta gcc aag aat aca aga aaa tca gac gct aag agc gtg Lys Leu Val Leu Ala Lys Asn Thr Arg Lys Ser Asp Ala Lys Ser Val 1 5	205					390					395					400	
Val Ala Glu Glu Val Gly Leu Ser Leu Asp Lys Val Lys Ass Val Ile  435  Lys Val Thr Lys Glu Pro Ile Ser Leu Glu Thr Pro Val Gly Ass Asp  450  Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Ass Ile Val Ser  460  Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Ass Ile Val Ser  470  Ser Ile Asp His Ile Met Arg Glu Asp Leu Lys Ala Gln Ile Glu Ser  485  Val Leu Asp Gln Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Met Arg  500  Phe Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Ile Gly  515  Lys Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser  530  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn  545  Tyr Leu Arg Ile  <210> 91  221> CDS  <222> (1)(237)  <400> 91  aaa cta gtt tta gcc aag aat aca aga aaa tca gac gct aag agc gtg  Lys Leu Val Leu Ala Lys Asn Thr Arg Lys Ser Asp Ala Lys Ser Val  1	•				405					410					412		
Lys Val Thr Lys Glu Pro Ile Ser Leu Glu Thr Pro Val Gly Asn Asp 450  Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Ile Val Ser 485  Ser Ile Asp His Ile Met Arg Glu Asp Lys Ala Gln Ile Glu Ser 485  Val Leu Asp Gln Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Met Arg 505  Phe Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Glu Ile Gly 515  Lys Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser 530  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 545  Tyr Leu Arg Ile <210> 91  <211> 237  <212> DNA  <213> Helicobacter pylori  <220>  <222> (1)(237)  <400> 91  aaa cta gtt tta gcc aag aat aca aga aaa tca gac gct aag agc gtg Lys Leu Val Leu Ala Lys Asn Thr Arg Lys Ser Asp Ala Lys Ser Val 1  5 gaa tta gag gat ttg tat cac gaa ttc agt gaa gat aag cgt tct att gcc ccc aca aac gcc cac aaa gac atg ctc aaa gcg gtg Phe Tyr Phe Ala Pro Thr Asn Ala His Lys Asp Met Leu Lys Ala Val  480  Asp Asp Clu Asp Lys Asp Met Leu Ser 470  480  Asp Lys Asn Ile Val Ser 480  490  495  490  495  495  Asp Lys Ash Val Ile Arg Met Arg 500  495  505  505  507  508  509  Fro Gln Tyr Gly Arg Ile Leu Arg Asn 560  540  555  555  560  560  577  588  589  599  599  599  599  599				420					425					430			
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No.	_	450					455					460					
Val Leu Asp Gln Leu Asn Glu Arg Glu Lys Ala Val Ile Arg S10  Phe Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Ile Gly 515  Lys Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser Ser 530  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 545  Tyr Leu Arg Ile  <210> 91  <211> 237  <212> DNA  <223> Helicobacter pylori  <220> <221> CDS  <222> (1)(237)  <400> 91  aaa cta gtt tta gcc aag aat aca aga aaa tca gcg gct aag agc gtg Lys Leu Val Leu Ala Lys Asn Thr Arg Lys Ser Asp Ala Lys Ser Val  1	466	_				470					4/5					400	
Phe Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Ile Gly 515  Lys Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser Ser 530  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 545  Tyr Leu Arg Ile 210> 91  221> 237  221> DNA  221> CDS  222> (1)(237)  4400> 91  aaa cta gtt tta gcc aag aat aca aga aaa tca gac gct aag agc gtg Lys Leu Val Leu Ala Lys Asn Thr Arg Lys Ser Asp Ala Lys Ser Val  1  5  10  15  16  17  18  18  19  19  10  15  10  15  16  17  18  18  19  19  10  10  11  15  10  15  10  15  10  15  10  15  10  15  10  15  10  15  10  15  10  15  10  15  10  15  10  11  15  10  15  10  15  11  11					485					490					490		
Lys Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser Ser 530 535 540  Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 545 550 555 560  Tyr Leu Arg Ile (210 > 91 (211 > 237 (212 > DNA (213 > Helicobacter pylori (220 > (221 > CDS (222 > (1) (237) (2400 > 91 (237 ) (2400 > 91 (237 ) (2400 > 91 (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240 ) (240				500					505					210			
Ala Ile Lys Lys Leu Arg Ser Pro Gln Tyr Gly Arg Ile Leu Arg Asn 545 550 560  Tyr Leu Arg Ile   <210> 91 <211> 237 <212> DNA <213> Helicobacter pylori <220> <221> CDS <222> (1)(237) <400> 91  aaa cta gtt tta gcc aag aat aca aga aaa tca gac gct aag agc gtg Lys Leu Val Leu Ala Lys Asn Thr Arg Lys Ser Asp Ala Lys Ser Val  1 5 10 15  gaa tta gag gat ttg tat cac gaa ttc agt gaa gat aag cgt tct att Glu Leu Glu Asp Leu Tyr His Glu Phe Ser Glu Asp Lys Arg Ser Ile  20 25 30  ttc tat ttt gcc ccc aca aac gcc cac aaa gac atg ctc aaa gcg gtg Phe Tyr Phe Ala Pro Thr Asn Ala His Lys Asp Met Leu Lys Ala Val			515					520					<b>3</b> 23				
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gaa tta gag gat ttg tat cac gaa ttc agt gaa gat aag cgt tct att Glu Leu Glu Asp Leu Tyr His Glu Phe Ser Glu Asp Lys Arg Ser Ile 20 25 30 ttc tat ttt gcc ccc aca aac gcc cac aaa gac atg ctc aaa gcg gtg Phe Tyr Phe Ala Pro Thr Asn Ala His Lys Asp Met Leu Lys Ala Val				tta Lev	gcc Ala	aag Lys	aat Asn	aca	aga Arg	Lys	Ser	Asp	gct	Lys	Ser	Vdl	48
Clu Leu Glu Asp Leu Tyr His Glu Phe Ser Glu Asp Lys Arg Ser Tie  20  25  30  ttc tat ttt gcc ccc aca aac gcc cac aaa gac atg ctc aaa gcg gtg Phe Tyr Phe Ala Pro Thr Asn Ala His Lys Asp Met Leu Lys Ala Val	- 1	i			5	•				10					13	٠.	96
ttc tat ttt gcc ccc aca aac gcc cac aaa gac atg ctc aaa gcg gtg Phe Tyr Phe Ala Pro Thr Asn Ala His Lys Asp Met Leu Lys Ala Val	gaa Glu	tta Leu	gag Glu	Asp	Leu	Tyr	His	Glu	Phe	Ser	Glu	Asp	Lys	Arg	Ser	Ile	
Phe Tyr Phe Ala Pro Thr Asn Ala His Lys Asp Met Leu Lys Ala Val		. +=+	. +++			aca	aac	gcc	cac	aaa	gac	atg	ctc	aaa	gcg	gtg	144
	Phe	Tyı	Phe	Ala	Pro	Thr	Asn	Ala 40	His	Lys	Asp	Met	45	i rys	. WIS	val	
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tat gcc cct ttt tat caa aag gct cga gcg ctc att aaa aag ggc gtt
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Tyr Ala Pro Phe Tyr Gln Lys Ala Arg Ala Leu Ile Lys Lys Gly Val
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get agg age aat ett gtt tta gaa ate eat aac agg ett tta ace eet
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Ala Arg Ser Asn Leu Val Leu Glu Ile His Asn Arg Leu Leu Thr Pro
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tat ttt agc gcg ggc gcg tta aac ggg acg ggt gtt gtg ggg ttg tta
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Tyr Phe Ser Ala Gly Ala Leu Asn Gly Thr Gly Val Val Gly Leu Leu
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Met Phe Asp Glu Ile Phe Tyr Asn Gln Asp Leu Glu Leu Thr Glu Gly
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Ala Arg Ser Asn Leu Val Leu Glu Ile His Asn Arg Leu Leu Thr Pro
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 aat agg gat tta gaa caa tgc aaa gag gat tta tta gcc gct aac gag
 Asn Arg Asp Leu Glu Gln Cys Lys Glu Asp Leu Leu Ala Ala Asn Glu
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His	Phe	Glu	Asp	Val	Asn	His	Leu 200	Leu	GIn	vaı	Leu	205	Ser	ъeл	Val	
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Tyr	Thr		Val	Met	Asp	Glu	Ile 40	Arg	Ile	Leu	Phe	Ala 45	Glu	Glr	Lys	
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GI	50		, 116	. Deu		55				- 2	60	)				

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 Val Ala Phe Cys Gly Gly Asp Glu Ala Met Val Cys Ala Ala Leu Leu
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 His Asp Val Val Glu Asp Thr Pro Cys Lys Ile Glu Thr Ile Glu Gln
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 Glu Phe Gly Gln Asp Val Ala Asn Leu Val Asp Ala Leu Thr Lys Ile
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 Thr Glu Ile Arg Lys Glu Glu Leu Gly Val Ser Ser Gln Asp Pro Arg
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gac	agc	gat	tou	Lys	Aen	Den	Pro	Lvs	Glu	Phe	Tvr	Glu	Leu	Ala	Lvs	
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Lys		Ala	Leu	Leu	Asn		GIU	Leu	Arg	ser	PTA	ASP	val	AST	ոչ	
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1405

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Val Ala Phe Cys Gly Gly Asp Glu Ala Met Val Cys Ala Ala Leu Leu
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His Asp Val Val Glu Asp Thr Pro Cys Lys Ile Glu Thr Ile Glu Gln
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Thr Glu Ile Arg Lys Glu Glu Leu Gly Val Ser Ser Gln Asp Pro Arg
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Met Val Val Ser Ala Leu Thr Phe Arg Lys Ile Leu Ile Ser Ala Ile
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Gln Asp Pro Arg Ala Leu Val Val Lys Ile Ser Asp Arg Leu His Asn
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Met Leu Thr Leu Asp Ala Leu Pro His Asp Lys Gln Val Arg Ile Ser
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Lys Glu Thr Leu Ala Val Tyr Ala Pro Ile Ala Ser Arg Leu Gly Met
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Pro Glu Glu Tyr Lys Asn Ile Lys Glu Tyr Leu His Lys Asn Lys Gln
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Ser Leu Leu Leu Lys Leu Asn Ala Phe Ala Ser Lys Leu Glu Lys Lys
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                    230
Leu Phe Asp Ser Gly Phe Ser His Ser Asp Phe Lys Leu Val Thr Arg
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Val Lys Arg Pro Tyr Ser Ile Tyr Leu Lys Met Gln Arg Lys Gly Ala
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Val Asn Ile Asp Glu Ile Leu Asp Leu Leu Ala Ile Arg Ile Leu Leu
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Lys Asn Pro Ile Asp Cys Tyr Lys Val Leu Gly Ile Ile His Leu Asn
                                            300
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Phe Lys Pro Ile Val Ser Arg Phe Lys Asp Tyr Ile Ala Leu Pro Lys
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Glu Asn Gly Tyr Lys Thr Ile His Thr Thr Ile Phe Asp Glu Ser Ser
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Val Tyr Glu Val Gln Ile Arg Thr Phe Asp Met His Met Gly Ala Glu
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Tyr Gly Asn Ser Ala His Trp Lys Tyr Lys Ala Gly Gly Val Asp His
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Arg Ile Ala Lys Ser Glu Leu Glu Lys Asp Thr Lys Leu Val Ser Ser
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Lys Ala Val Gln Ile Ser Leu Asn Asn Pro Asn Leu Lys Asp Leu Glu
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                                                     110
cgc acc aaa gcc tta ttg aaa gat tgc gat gtg gtg ttt atc ata agc
                                                                    384
Arg Thr Lys Ala Leu Leu Lys Asp Cys Asp Val Val Phe Ile Ile Ser
                             120
                                                 125
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tct tct aat cag ttt tta acg gag agc gat atg agt ttg ttt gac agg
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Ser Ser Asn Gln Phe Leu Thr Glu Ser Asp Met Ser Leu Phe Asp Arg
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                         135
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Ala Asp Ser Ala Val Leu Ser Met Ser Glu Val Glu Lys Ser Arg His
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 cac etc ecc aca gee tta gaa aac geg caa aaa tee ett tea tet tet
                                                                    576
 His Leu Pro Thr Ala Leu Glu Asn Ala Gln Lys Ser Leu Ser Ser Ser
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                                                     190
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 Leu Asn Lys Thr Met Glu Ala Leu Ile Gln Thr Asn Pro Asn Gln Arg
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 Gly Ile Phe Glu Lys Ala Ile Lys Asn Gly Val Ile Leu Thr Ser Gly
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His Leu Pro Thr Ala Leu Glu Asn Ala Gln Lys Ser Leu Ser Ser Ser
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Leu Asn Lys Thr Met Glu Ala Leu Ile Gln Thr Asn Pro Asn Gln Arg
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Ala Cys Phe Ser Met Tyr Lys Asp Phe Lys Asn Gln Ala Ser Trp Glu
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Ser Lys Lys Glu Glu Cys Tyr Asn Ala Trp Arg Asn Leu Thr Asn Ala
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cac cac cat caa gac gat etc gct att cag tat tta cca gcc gtg cgc
His His His Gln Asp Asp Leu Ala Ile Gln Tyr Leu Pro Ala Val Arg
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Asn	Asp	Leu	Val	Ser	Ile	Gly	Thr	Glu	Glu	Leu	TTE	rys	Leu	ATA	Arg	
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cgt	gtc	aat	999	Ala	Mot	Lou	Agn	Tur	Leu	Ara	Ser	Leu	Asp	Val	Ile	
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Arg	Tyr	Glu	ı Ser	Ala	Leu	Asn	Asp	Ser	Phe	Trp	GIY	Tyr	ATS	r rys	Thr	
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Lys	s His			Glu	His	Gly	Lys	GIU	PIO	ser	. ASP	125	yı	. Det	ı Ala	
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Ile Gln Leu Tyr Tyr Phe Glu Glu Leu Asn Leu Ser Glu Ile Lys Glu
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Ser Leu Pro Gln Phe Gly Gly Met Tyr Ala Gly Asp Met Ser Arg Lys
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cgc cct tta aaa ttt gat gaa ttt atc cat aaa aat tgc cag ttc ctt
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atc aag tta gtg gtg gct aga ggt gaa agg gtg ctc atc acc acg ctc
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 Ile Lys Leu Val Val Ala Arg Gly Glu Arg Val Leu Ile Thr Thr Leu
                                     170
                 165
 act aaa aaa atg gca gaa gaa ttg tgc aaa tat tat gct gaa tgg ggc
 Thr Lys Lys Met Ala Glu Glu Leu Cys Lys Tyr Tyr Ala Glu Trp Gly
                                 185
            180
 ttg aag gcg cgt tac atg cat agt gaa att gat gcg att gaa agg aat
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 Leu Lys Ala Arg Tyr Met His Ser Glu Ile Asp Ala Ile Glu Arg Asn
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 cac atc atc cgc tct tta agg ctt aaa gaa ttt gac att tta ata ggg
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	Asn	Leu	Leu	Arg	GIU	Grå	200			235					240	
225					230						200	agt	naa	aca	age	768
gcg	atc	atg	gat	gcg	gat	aaa	gaa	ggg	בננ	cta	agg	agt	Gla	mb-	ege Co-	, 00
gcg Ala	Ile	Met	Asp	Ala	Asp	Lys	Glu	Gly	Phe	Leu	Arg	Ser	GIU	* * * * *	Ser	
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			200		aaa	cga	acc	act	aga	aac	gct	aat	ggc	aag	gtt	816
CLC	att	Caa	acc	Met	999	7-4	λla	Δla	Ara	Asn	Ala	Asn	Glv	Lys	Val	
Leu	Ile	GIn	Thr	met	GTA	ALG	AT G	265					270	•		
			260					203						+++	aaa	864
tta	tta	tac	gct	aaa	aag	atc	act	caa	agc	atg	Caa	aaa	gcc	Db -	gay Cl.	004.
Leu	Leu	Tvr	Ala	Lys	Lys	Ile	Thr	Gln	Ser	Met	GIU	пåэ	ATA	Pne	GIU	
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acc	acc	Com	T	Arg	Ara	Δla	Lvs	Gln	Glu	Glu	Phe	Asn	Lys	Ile	His	
тте		Ser	IÀT	My	AL 9	295	_,_				300		_			
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aac	atc	acc	CCC	aaa	acc	gtt	acg	cgc	31-	Tou	Clu	C1	Clu	Len	Lve	•
Asn	Ile	Thr	Pro	Lys	Thr	Vai	Thr	Arg	ATA	Leu	GIU	GIU	GIU	Deu	220	
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Tan	aya aya	700	200	Glu	Tle	Ara	Ile	Ala	Lys	Ala	Leu	Lys	Lys	Asp	Lys	•
Leu	Arg	ASP	Asp	325		9			330			_		335		
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		.522					-									1134
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Leu	Lys		Arg	Tyr	Met	His	Ser	Glu	Ile	Asp	Ala	11e 205	Glu	Arg	Asn	
His	Ile	195 Ile	Arg	Ser	Leu	Arg	200 Leu	Lys	Glu	Phe	Asp 220		Leu	Ile	Gly	
<b>~</b> 1.	210 Asn	T 011	Lou	Ara	Glu	215 Glv	Leu	Asp	Leu	Pro	Glu	Val	Ser	Leu	Val	
200					230					233					210	•
Ala	Ile			215					230					233		
	Ile		260	Met				265					210			
	Leu	275	Ala				280					203				
	Thr 290	Ser				295					300					
Asn	Ile	Thr	Pro	Lys	Thr	Val	Thr	Arg	Ala	Leu	Glu	Glu	Glu	Leu	Lys 320	
205	Arg				310					212					320	
				325					330					333		
	Pro		310					345					330			
	Arg	355					360				GIU	365	Met	Arg	ren	
Arg	Asp 370	Glu	Ile	Ala	Gln	Leu 375	Arg	Thr	Leu							
	0> 1															
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<21		elic	UDaC.	LEI ;	py ro.											
	1> C	DS														
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	. ,	_,	(330	,												
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qaa Glu l ctt Leu gct Ala	0> 1 tcc Ser aag Lys aac	tta Leu cag Gln cag Gln 35	cga Arg caa Gln 20 caa Gln	gcc Ala 5 tcg Ser gct Ala	caa Gln atc	Lys act Thr cag Gln	tta Leu cag Gln	gag Glu 25 tta Leu	10 gat Asp gac Asp	ttg Leu aag Lys	agg Arg caa Gln	aat Asn aat Asn 45	gag Glu 30 aaa Lys	15 att Ile gag	cac His atg Met	96 144 192
ctt Lev gct Ala agt	tcc Ser aag Lys aac Asn	cag Gln cag Gln tta	cga Arg caa Gln 20 caa Gln ttg	gcc Ala 5 tcg Ser gct Ala acc	caa Gln atc Ile aag	Lys act Thr cag Gln tta	tta Leu cag Gln 40 agc Ser	gag Glu 25 tta Leu cag Gln	gat Asp gac Asp gac Asp	ttg Leu aag Lys ttg	agg Arg caa Gln gtt Val	aat Asn aat Asn 45 tca Ser	gag Glu 30 aaa Lys caa	15 att	cac His atg Met	96 144 192
ctt Lev gct Ala agt	tcc Ser aag Lys aac Asn gaa Glu	cag Gln cag Gln 35 tta	cga Arg caa Gln 20 caa Gln ttg	gcc Ala 5 tcg Ser gct Ala acc Thr	caa Gln atc Ile aag Lys	Lys act Thr cag Gln tta	tta Leu cag Gln 40 agc Ser	gag Glu 25 tta Leu cag Gln	gat Asp gac Asp gat Asp	ttg Leu aag Lys ttg Leu	agg Arg caa Gln gtt Val 60 aaa	aat Asn aat Asn 45 tca Ser	gag Glu 30 aaa Lys caa Gln	15 att Ile	cac His atg Met gcc Ala	96 144 192 240
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ctt Get Lev gct Ala agt tta Lev	tcc Ser aag Lys aac Asn Glu 50 a atc	tta Leu cag Gln cag Gln 35 tta Leu caa	cga Arg caa Gln 20 caa Gln ttg Leu	gcc Ala 5 tcg Ser gct Ala acc Thr	caa Gln atc Ile aag Lys ctc Leu 70	Lys act Thr cag Gln tta Leu 55 aaa Lys	tta Leu cag Gln 40 agc Ser gaa Glu	gag Glu 25 tta Leu cag Gln caa Gln	gat Asp gac Asp gat Asp gat Glu	ttg Leu aag Lys ttg Leu gaa Glu 75	agg Arg caa Gln gtt Val 60 aaa Lys	aat Asn aat Asn 45 tca Ser gct Ala	gag Glu 30 aaa Lys caa Gln gaa	15 att Ile Glu atc Ile Lys	cac His atg Met gcc Ala ccg Pro 80	96 144 192 240 288
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ctt Let gct Ala agt tta Let Ctc	tcc Ser aag Lys aac Asn 50 a atc 50 a atc 50 a atc	tta Leu cag Gln cag Gln 35 tta Leu cag School	cga Arg caa Gln caa Gln ttg Leu Lys	gcc Alas 5 tcg Ser gct Ala acc Thr gct Ala 95	caa Gln atc Ile aag Lys ctc Leu 70 ccg Pro	Lys act Thr cag Gln tta Leu 55 aaa Lys gct	tta Leu Cag Gln 40 agc Ser gaa Glu aat	gag Glu 25 tta Leu cag Gln caa Gln aaa Lys	gat Asp gat Asp gat Asp gag Glu acc Thr	ttg Leu aag Lys ttg Leu gaa Glu 75	agg Arg caa Gln gtt Val 60 aaa Lys	aat Asn asn 45 tca Ser gct Ala	gag Glu 30 aaa Lys caa Gln gaa Glu	15 att Ile gag Glu atc Ile aac Lys Ala	cac His atg Met gcc Ala ccg Pro 80 gaa Glu	96 144 192 240 288
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aag cat ttt atg gac aga ttt tta aag aat aac gct aag gcg agc gtg
                                                                    288
Lys His Phe Met Asp Arg Phe Leu Lys Asn Asn Ala Lys Ala Ser Val
                                      90
                  85
aaa gac ttt atg tct agt aag gag ttt gtc gct aaa tac cga tac acc
                                                                    336
Lys Asp Phe Met Ser Ser Lys Glu Phe Val Ala Lys Tyr Arg Tyr Thr
                                                     110
                                 105
ccc aag caa aat aca gaa aga gcg aaa aag ctg caa tcg tat tta gag
                                                                    384
Pro Lys Gln Asn Thr Glu Arg Ala Lys Lys Leu Gln Ser Tyr Leu Glu
                                                 125
                             120
aat aag cgc gat ttt ata ggg ttt gtt caa gcg ctt aac tct tta aaa
                                                                    432
Asn Lys Arg Asp Phe Ile Gly Phe Val Gln Ala Leu Asn Ser Leu Lys
                                             140
                         135
 gac aac ccg caa gat cct ttt tta ccc aat gaa gaa acg agc ttt ttg
                                                                    480
 Asp Asn Pro Gln Asp Pro Phe Leu Pro Asn Glu Glu Thr Ser Phe Leu
                                         155
                     150
                                                                    498
 gtg ttc gct aat gag cct
 Val Phe Ala Asn Glu Pro
                 165
 <210> 116
 <211> 166
 <212> PRT
 <213> Helicobacter pylori
 <400> 116
Phe Lys Pro Phe Lys Asp Ala Phe Tyr Arg Asp Phe Asn His Asn Glu
                                      10
 Gln Lys Leu Leu Ile Gly Ala Ala Lys Ser Gly Cys Ile Gln Ser Ser
                                  25
 Ala Asp Lys Leu Ala Gln Leu Lys Thr Arg Leu Leu Tyr Trp Gln Asp
 Lys Ser Val Lys Val Asp Trp Asp Lys Pro Ile Leu Ile Lys Asp Phe
 Phe Lys Gly Asn Asn Tyr Leu Tyr Arg Arg Phe Cys Phe Leu Leu Gly
```

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75
Lys His Phe Met Asp Arg Phe Leu Lys Asn Asn Ala Lys Ala Ser Val
                                     90
Lys Asp Phe Met Ser Ser Lys Glu Phe Val Ala Lys Tyr Arg Tyr Thr
                                                    110
                                105
            100
Pro Lys Gln Asn Thr Glu Arg Ala Lys Lys Leu Gln Ser Tyr Leu Glu
                                                125
                            120
Asn Lys Arg Asp Phe Ile Gly Phe Val Gln Ala Leu Asn Ser Leu Lys
                                            140
                        135
Asp Asn Pro Gln Asp Pro Phe Leu Pro Asn Glu Glu Thr Ser Phe Leu
                    150
Val Phe Ala Asn Glu Pro
                165
<210> 117
<211> 399
<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(399)
<400> 117
ctc gct ttg aat gag ttg aat ccg ggc gaa tgg gtg gtg cat gat gat
Leu Ala Leu Asn Glu Leu Asn Pro Gly Glu Trp Val Val His Asp Asp
                                                          15
                  5
                                     10
tat ggg gtg ggc gtg ttt tct caa tta gtc cag cac agc gtt tta ggg
                                                                   96
Tyr Gly Val Gly Val Phe Ser Gln Leu Val Gln His Ser Val Leu Gly
                                                      30 .
                                 25
agc aag agg gat ttt tta gaa atc gct tat ttg ggc gaa gac aaa ctg
Ser Lys Arg Asp Phe Leu Glu Ile Ala Tyr Leu Gly Glu Asp Lys Leu
                              40
        35
ctg tta ccg gta gaa aac ttg cat ctc atc gct cgc tat gtg gcg caa
                                                                   192
Leu Leu Pro Val Glu Asn Leu His Leu Ile Ala Arg Tyr Val Ala Gln
                                           . 60
age gat age gtg cea get aaa gae egg eta ggg aaa ggg age ttt ett
                                                                    240
Ser Asp Ser Val Pro Ala Lys Asp Arg Leu Gly Lys Gly Ser Phe Leu
                     70
aaa tta aaa gct aaa gtc agg act aag ctt tta gag att gct agc aag
                                                                    288
Lys Leu Lys Ala Lys Val Arg Thr Lys Leu Leu Glu Ile Ala Ser Lys
                 85
atc att gaa tta gcg gct gaa cgc aat ttg atc ttg ggt aaa aag atg
                                                                   336
Ile Ile Glu Leu Ala Ala Glu Arg Asn Leu Ile Leu Gly Lys Lys Met
                                 105
            100
gat gtg cat tta gcg gag ttg gaa gtc ttt aaa tcg cat gcg ggg ttt
                                                                    384
Asp Val His Leu Ala Glu Leu Glu Val Phe Lys Ser His Ala Gly Phe
                                                 125
                             120
        115
                                                                    399
gaa tac acc agc gat
Glu Tyr Thr Ser Asp
    130
<210> 118
<211> 133
<212> PRT
<213> Helicobacter pylori
<400> 118
Leu Ala Leu Asn Glu Leu Asn Pro Gly Glu Trp Val Val His Asp Asp
                                      10
Tyr Gly Val Gly Val Phe Ser Gln Leu Val Gln His Ser Val Leu Gly
                                  25
             20
Ser Lys Arg Asp Phe Leu Glu Ile Ala Tyr Leu Gly Glu Asp Lys Leu
                            40
Leu Leu Pro Val Glu Asn Leu His Leu Ile Ala Arg Tyr Val Ala Gln
                                              60
                          55
```

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Ser Asp Ser Val Pro Ala Lys Asp Arg Leu Gly Lys Gly Ser Phe Leu
                     70
Lys Leu Lys Ala Lys Val Arg Thr Lys Leu Leu Glu Ile Ala Ser Lys
                                     90
                85
Ile Ile Glu Leu Ala Ala Glu Arg Asn Leu Ile Leu Gly Lys Lys Met
                                                 . 110
                                105
Asp Val His Leu Ala Glu Leu Glu Val Phe Lys Ser His Ala Gly Phe
                            120
       115
Glu Tyr Thr Ser Asp
  130
<210> 119
<211> 426
<212> DNA
<213> Helicobacter pylori
<221> CDS
<222> (1)..(426)
<400> 119
gtt tta aac gca ccc atc act tta gaa gac att caa gaa tta agc tcc
Val Leu Asn Ala Pro Ile Thr Leu Glu Asp Ile Gln Glu Leu Ser Ser
                                     10
aat gcg ggg gat atg gat ttg caa aag ctc att tta ggg ctt ttt tta
                                                                   96
Asn Ala Gly Asp Met Asp Leu Gln Lys Leu Ile Leu Gly Leu Phe Leu
                                 25
aaa aaa agt gcg ctt gat att tat gat tat ttg tta aaa gag ggc aaa
Lys Lys Ser Ala Leu Asp Ile Tyr Asp Tyr Leu Leu Lys Glu Gly Lys
                             40
                                                 45
         35
aaa gat gcg gat att tta agg ggg tta gag cgc tat ttt tac caa ctt
                                                                   192
Lys Asp Ala Asp Ile Leu Arg Gly Leu Glu Arg Tyr Phe Tyr Gln Leu
                                             60
                         55
ttt tta ttt ttc gct cat att aaa acg acc ggt tta atg gac gct aaa
                                                                   240
Phe Leu Phe Phe Ala His Ile Lys Thr Thr Gly Leu Met Asp Ala Lys
                                         75
                     70
gag gtt tta ggc tac gct ccc cct aaa gaa att gcc gaa aat tac gct
                                                                   288
Glu Val Leu Gly Tyr Ala Pro Pro Lys Glu Ile Ala Glu Asn Tyr Ala
                                     90
                                                         95
                 85
                                                                   336
aaa aac gcc ttg cgt ttg aaa gaa gcc ggc tat aag agg gtt ttt gaa
Lys Asn Ala Leu Arg Leu Lys Glu Ala Gly Tyr Lys Arg Val Phe Glu
                                105
                                                     110
            100
att ttt agg tta tgg cac att caa agc atg caa ggg caa aag gaa ttg
                                                                   384
Ile Phe Arg Leu Trp His Ile Gln Ser Met Gln Gly Gln Lys Glu Leu
                                                125
                            120
       115
ggc ttt ttg tat ttg acc tcc att caa aaa atc att aac ccc
                                                                   426
Gly Phe Leu Tyr Leu Thr Ser Ile Gln Lys Ile Ile Asn Pro
    130
                        135
<210> 120
<211> 142
<212> PRT
<213> Helicobacter pylori
<400> 120
Val Leu Asn Ala Pro Ile Thr Leu Glu Asp Ile Gln Glu Leu Ser Ser
                                     10
Asn Ala Gly Asp Met Asp Leu Gln Lys Leu Ile Leu Gly Leu Phe Leu
Lys Lys Ser Ala Leu Asp Ile Tyr Asp Tyr Leu Leu Lys Glu Gly Lys
                             40
Lys Asp Ala Asp Ile Leu Arg Gly Leu Glu Arg Tyr Phe Tyr Gln Leu
                         55
Phe Leu Phe Phe Ala His Ile Lys Thr Thr Gly Leu Met Asp Ala Lys
                     70
Glu Val Leu Gly Tyr Ala Pro Pro Lys Glu Ile Ala Glu Asn Tyr Ala
```

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90
                85
Lys Asn Ala Leu Arg Leu Lys Glu Ala Gly Tyr Lys Arg Val Phe Glu
                               105
           100
Ile Phe Arg Leu Trp His Ile Gln Ser Met Gln Gly Gln Lys Glu Leu
                           120
       115
Gly Phe Leu Tyr Leu Thr Ser Ile Gln Lys Ile Ile Asn Pro
                       135
   130
<210> 121
<211> 297
<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(297)
<400> 121
gaa gaa tgc ggc acg ctt tta gaa ttg agg gaa aaa att tcg ttg ttt
Glu Glu Cys Gly Thr Leu Leu Glu Leu Arg Glu Lys Ile Ser Leu Phe
                 5
tta gag cca aag gat att gtt aaa act tat gaa aat gaa gat ttt aaa
                                                                 96
Leu Glu Pro Lys Asp Ile Val Lys Thr Tyr Glu Asn Glu Asp Phe Lys
                                25
             20
gag cgt tgt tta gcg ctt ttt aac gct cta aca agc atg gat ttt caa
                                                                 144
Glu Arg Cys Leu Ala Leu Phe Asn Ala Leu Thr Ser Met Asp Phe Gln
                                                45
                             40
         35
Ala Tyr Lys Asp Phe Glu Ser Phe Lys Lys Glu Ala Met Arg Leu Ser
                                            60
                         55
cag ctt aag ggt aag gat ttt ttc aaa cct ttg cgc atc ctt tta acc
                                                                 240
Gln Leu Lys Gly Lys Asp Phe Phe Lys Pro Leu Arg Ile Leu Leu Thr
                                        75
                     70
 65
ggg aac tcg cat ggc gtt gaa ttg cct ttg att ttc ccc tat atc caa
                                                                 288
Gly Asn Ser His Gly Val Glu Leu Pro Leu Ile Phe Pro Tyr Ile Gln
                 85
                                                                 297
agc cat cat
Ser His His
 <210> 122
 <211> 99
 <212> PRT
 <213> Helicobacter pylori
 <400> 122
 Glu Glu Cys Gly Thr Leu Leu Glu Leu Arg Glu Lys Ile Ser Leu Phe
                                    10
  1
 Leu Glu Pro Lys Asp Ile Val Lys Thr Tyr Glu Asn Glu Asp Phe Lys
 Glu Arg Cys Leu Ala Leu Phe Asn Ala Leu Thr Ser Met Asp Phe Gln
                             40
 Ala Tyr Lys Asp Phe Glu Ser Phe Lys Lys Glu Ala Met Arg Leu Ser
                         55
 Gln Leu Lys Gly Lys Asp Phe Phe Lys Pro Leu Arg Ile Leu Leu Thr
                                         75
                     70
 Gly Asn Ser His Gly Val Glu Leu Pro Leu Ile Phe Pro Tyr Ile Gln
 Ser His His
 <210> 123
 <211> 42
 <212> DNA
 <213> Helicobacter pylori
 <220>
 <221> CDS
 <222> (1)..(42)
 <400> 123
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ccc caa atc gta gct aaa gat ttt tta gaa aga tta ggg tta
                                                                   42
Pro Gln Ile Val Ala Lys Asp Phe Leu Glu Arg Leu Gly Leu
 1
<210> 124
<211> 14
<212> PRT
<213> Helicobacter pylori
<400> 124
Pro Gln Ile Val Ala Lys Asp Phe Leu Glu Arg Leu Gly Leu
 1
<210> 125
<211> 84
<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(84)
<400> 125
aag aaa gcg att gaa aat aac cag tat aaa atc aac ttg cat gag act
Lys Lys Ala Ile Glu Asn Asn Gln Tyr Lys Ile Asn Leu His Glu Thr
                                      10
 1
                                                                   84
tct cac aaa atg gca aag gat tta ttg ggg ata agc
Ser His Lys Met Ala Lys Asp Leu Leu Gly Ile Ser
<210> 126
<211> 28
<212> PRT
<213> Helicobacter pylori
<400> 126
Lys Lys Ala Ile Glu Asn Asn Gln Tyr Lys Ile Asn Leu His Glu Thr
                                     10
Ser His Lys Met Ala Lys Asp Leu Leu Gly Ile Ser
             20
<210> 127
<211> 356
<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS '
<222> (1)..(354)
cac att tat gaa aaa gaa gtg gat gct agg gag ctt aag cat ggt gtg
His Ile Tyr Glu Lys Glu Val Asp Ala Arg Glu Leu Lys His Gly Val
                                      10
gaa gaa ttt acc gct gat att cct gat gtg aaa gaa gaa gcg ctc gct
                                                                   96
Glu Glu Phe Thr Ala Asp Ile Pro Asp Val Lys Glu Glu Ala Leu Ala
cat ctt gat gaa agc ggg atc gtt aaa gtc ggt act tat gtg agc gct
                                                                   144
His Leu Asp Glu Ser Gly Ile Val Lys Val Gly Thr Tyr Val Ser Ala
                             40
                                                  45
         35
ggc atg att ttg gtg ggc aaa act tct cct aaa ggc gag att aaa agc
                                                                   192
Gly Met Ile Leu Val Gly Lys Thr Ser Pro Lys Gly Glu Ile Lys Ser
acg cct gaa gag cgg ctt tta agg gct att ttt ggg gat aaa gcc ggg
                                                                   240
Thr Pro Glu Glu Arg Leu Leu Arg Ala Ile Phe Gly Asp Lys Ala Gly
                     70
cat gtg gtc aat aag agt ttg tat tgc cct ccc agt ttg gaa ggc acg
                                                                   288
His Val Val Asn Lys Ser Leu Tyr Cys Pro Pro Ser Leu Glu Gly Thr
                                      90
gtg att gat gtg aaa gtc ttc act aaa aaa ggc tat gag aaa gac gcg
                                                                   336
Val Ile Asp Val Lys Val Phe Thr Lys Lys Gly Tyr Glu Lys Asp Ala
```

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110
                                105
            100
                                                                   356
cga gtt ttg agc gcg tat ga
Arg Val Leu Ser Ala Tyr
        115
<210> 128
<211> 118
<212> PRT
<213> Helicobacter pylori
<400> 128
His Ile Tyr Glu Lys Glu Val Asp Ala Arg Glu Leu Lys His Gly Val
                                     10
Glu Glu Phe Thr Ala Asp Ile Pro Asp Val Lys Glu Glu Ala Leu Ala
                                 25
             20
His Leu Asp Glu Ser Gly Ile Val Lys Val Gly Thr Tyr Val Ser Ala
                             40
         35
Gly Met Ile Leu Val Gly Lys Thr Ser Pro Lys Gly Glu Ile Lys Ser
                         55
Thr Pro Glu Glu Arg Leu Leu Arg Ala Ile Phe Gly Asp Lys Ala Gly
                                          75
                     70
His Val Val Asn Lys Ser Leu Tyr Cys Pro Pro Ser Leu Glu Gly Thr
                                      90
                 85
Val Ile Asp Val Lys Val Phe Thr Lys Lys Gly Tyr Glu Lys Asp Ala
                                 105
            100
Arg Val Leu Ser Ala Tyr
        115
<210> 129
<211> 698
<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
 <222> (1)..(696)
 <400> 129
tat aag ccc tac acc cca agc aga cgc ttc atg tcg gtg ttg gac tct
 Tyr Lys Pro Tyr Thr Pro Ser Arg Arg Phe Met Ser Val Leu Asp Ser
                                      10
 aaa gac att acc gca aaa agc agt gtc aaa ggc tta ctc act aag ctt
  1
                                                                    96
Lys Asp Ile Thr Ala Lys Ser Ser Val Lys Gly Leu Leu Thr Lys Leu
                                  25
              20
 aaa gca aca gca ggg aga aac aat aac ggg cgc atc acc agc cgc cac
                                                                    144
 Lys Ala Thr Ala Gly Arg Asn Asn Gly Arg Ile Thr Ser Arg His
                              40
          35
 aaa gag aga ggg gct aaa aaa ctc tat cgc att att gat ttc aag cgc
                                                                    192
 Lys Glu Arg Gly Ala Lys Lys Leu Tyr Arg Ile Ile Asp Phe Lys Arg
                                              60
                          55
 aat aaa tac aat att gaa ggg aaa gtg gct gcg att gag tat gat cct
                                                                    240
 Asn Lys Tyr Asn Ile Glu Gly Lys Val Ala Ala Ile Glu Tyr Asp Pro
                      70
 tac aga aat gcg cgc atc gct ctt gta gtc tat cct gat ggg gac aaa
                                                                    288
 Tyr Arg Asn Ala Arg Ile Ala Leu Val Val Tyr Pro Asp Gly Asp Lys
                                      90
                  85
 cgc tat att tta cag cca agc ggt ttg aaa gtg ggc gat agc gtt atc
 Arg Tyr Ile Leu Gln Pro Ser Gly Leu Lys Val Gly Asp Ser Val Ile
                                 105
             100
 gct gct gaa ggc ggt ttg gat att aaa gtg ggc ttt gcg atg aag tta
                                                                    384
 Ala Ala Glu Gly Gly Leu Asp Ile Lys Val Gly Phe Ala Met Lys Leu
                             120
 ada aat atc ccc ata gga acg gtg gtg cat aat att gaa atg cat cca
                                                                    432
 Lys Asn Ile Pro Ile Gly Thr Val Val His Asn Ile Glu Met His Pro
                         135
     130
 ggg gct ggc ggg caa tta gcc aga agc gca gga atg agc gct caa atc
                                                                    480
```

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Gly Ala Gly Gly Gln Leu Ala Arg Ser Ala Gly Met Ser Ala Gln Ile
                                        155
                    150
atg ggt aga gaa aat aaa tac acc att att agg atg cca agc tct gaa
                                                                   528
Met Gly Arg Glu Asn Lys Tyr Thr Ile Ile Arg Met Pro Ser Ser Glu
                                    170
                165
atg cgc tac att cta agc gaa tgt atg gcg agt gtt ggc gtg gta ggg
                                                                  576
Met Arg Tyr Ile Leu Ser Glu Cys Met Ala Ser Val Gly Val Val Gly
                                185
            180
aat gag gat ttt atc aat gtc tct atc ggt aag gca ggg cgt aac cgc
                                                                   624
Asn Glu Asp Phe Ile Asn Val Ser Ile Gly Lys Ala Gly Arg Asn Arg
                                                205
                            200
        195
cac aga ggg atc cgc cca caa act cgt ggt agc gcg atg aac cca gtg
                                                                   672
His Arg Gly Ile Arg Pro Gln Thr Arg Gly Ser Ala Met Asn Pro Val
                        215
gat cac ccg cat ggt ggg ggt gag gg
                                                                   698
Asp His Pro His Gly Gly Glu
225
<210> 130
<211> 232
<212> PRT
<213> Helicobacter pylori
<400> 130
Tyr Lys Pro Tyr Thr Pro Ser Arg Arg Phe Met Ser Val Leu Asp Ser
                                     10
Lys Asp Ile Thr Ala Lys Ser Ser Val Lys Gly Leu Leu Thr Lys Leu
                                 25.
            20
Lys Ala Thr Ala Gly Arg Asn Asn Gly Arg Ile Thr Ser Arg His
         35
Lys Glu Arg Gly Ala Lys Lys Leu Tyr Arg Ile Ile Asp Phe Lys Arg
                         55
Asn Lys Tyr Asn Ile Glu Gly Lys Val Ala Ala Ile Glu Tyr Asp Pro
                     70
                                         75
Tyr Arg Asn Ala Arg Ile Ala Leu Val Val Tyr Pro Asp Gly Asp Lys
                                     90
                 85
Arg Tyr Ile Leu Gln Pro Ser Gly Leu Lys Val Gly Asp Ser Val Ile
            100
Ala Ala Glu Gly Gly Leu Asp Ile Lys Val Gly Phe Ala Met Lys Leu
                            120
                                                125
Lys Asn Ile Pro Ile Gly Thr Val Val His Asn Ile Glu Met His Pro
                        135
                                            140
Gly Ala Gly Gly Gln Leu Ala Arg Ser Ala Gly Met Ser Ala Gln Ile
                                        155
                    150
Met Gly Arg Glu Asn Lys Tyr Thr Ile Ile Arg Met Pro Ser Ser Glu
                                    170
               165
Met Arg Tyr Ile Leu Ser Glu Cys Met Ala Ser Val Gly Val Val Gly
                                185
           180
Asn Glu Asp Phe Ile Asn Val Ser Ile Gly Lys Ala Gly Arg Asn Arg
                                                205
       195
                            200
His Arg Gly Ile Arg Pro Gln Thr Arg Gly Ser Ala Met Asn Pro Val
                        215
   210
Asp His Pro His Gly Gly Glu
                    230
225
<210> 131
<211> 528
<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(528)
<400> 131
tac gat tgg atc aag gaa ttt gtg cgc gat caa gga gag ttt atc gcc
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<211> 263

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Tyr Asp Trp Ile Lys Glu Phe Val Arg Asp Gln Gly Glu Phe Ile Ala
                                     10
caa caa agc ggg tgg ctg gaa tta gag cga tca agc tat gcc aaa ctc
                                                                  96
Gln Gln Ser Gly Trp Leu Glu Leu Glu Arg Ser Ser Tyr Ala Lys Leu
                                 25
atc gcg caa acc atc tcg cat gtg ctt aat ggc gga tcg ctg ttg gtg
Ile Ala Gln Thr Ile Ser His Val Leu Asn Gly Gly Ser Leu Leu Val
                             40
age geg gat tet tet agg cae tgg ttt tta aac tae att ett tet aac
Ser Ala Asp Ser Ser Arg His Trp Phe Leu Asn Tyr Ile Leu Ser Asn
                                             60
                         55
cta aac ccc aaa gat tta aaa gag cgc ccc tta ttg tcc gtc att gat
Leu Asn Pro Lys Asp Leu Lys Glu Arg Pro Leu Leu Ser Val Ile Asp
                                         75
                     70
ttt aac gct tct tct ttc tac ccc aaa aac gat gcg aat ctc tct cta
                                                                   288
Phe Asn Ala Ser Ser Phe Tyr Pro Lys Asn Asp Ala Asn Leu Ser Leu
                 85
gcc acc ata gag atg act tat caa aac ccc atg ttt tgg cat gtt ggg
                                                                   336
Ala Thr Ile Glu Met Thr Tyr Gln Asn Pro Met Phe Trp His Val Gly
                                105
            100
aaa att gaa aat gaa ggc tta aaa acg ata cta ttg agt aaa atc cct
Lys Ile Glu Asn Glu Gly Leu Lys Thr Ile Leu Leu Ser Lys Ile Pro
                                                125
                            120
agt ttt tta tgg ctt ttt gaa gag ctt aaa gaa gat tgc ttg ctt tta
                                                                   432
Ser Phe Leu Trp Leu Phe Glu Glu Leu Lys Glu Asp Cys Leu Leu
                        135
aaa gag cat gac agc ttg ctg gat tat aaa tta ttg cag ctc ttc aaa
                                                                   480
Lys Glu His Asp Ser Leu Leu Asp Tyr Lys Leu Leu Gln Leu Phe Lys
                                        155
                    150
ctc ttt gaa aac gcg ctt ttt agc gtg cta tac aat aag gtt act ctg
                                                                   528
Leu Phe Glu Asn Ala Leu Phe Ser Val Leu Tyr Asn Lys Val Thr Leu
                165
<210> 132
<211> 176
<212> PRT
<213> Helicobacter pylori
<400> 132
Tyr Asp Trp Ile Lys Glu Phe Val Arg Asp Gln Gly Glu Phe Ile Ala
Gln Gln Ser Gly Trp Leu Glu Leu Glu Arg Ser Ser Tyr Ala Lys Leu
Ile Ala Gln Thr Ile Ser His Val Leu Asn Gly Gly Ser Leu Leu Val
Ser Ala Asp Ser Ser Arg His Trp Phe Leu Asn Tyr Ile Leu Ser Asn
Leu Asn Pro Lys Asp Leu Lys Glu Arg Pro Leu Leu Ser Val Ile Asp
                                         75
Phe Asn Ala Ser Ser Phe Tyr Pro Lys Asn Asp Ala Asn Leu Ser Leu
                                     90
Ala Thr Ile Glu Met Thr Tyr Gln Asn Pro Met Phe Trp His Val Gly
                                105
Lys Ile Glu Asn Glu Gly Leu Lys Thr Ile Leu Leu Ser Lys Ile Pro
                            120
                                                125
Ser Phe Leu Trp Leu Phe Glu Glu Leu Lys Glu Asp Cys Leu Leu
                                            140
                        135
Lys Glu His Asp Ser Leu Leu Asp Tyr Lys Leu Leu Gln Leu Phe Lys
                                        155
                    150
Leu Phe Glu Asn Ala Leu Phe Ser Val Leu Tyr Asn Lys Val Thr Leu
                                    170
<210> 133
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<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(261)
<400> 133
ttg gcg cta gtc aaa caa aat cct aaa gtt agt ctc ata gag tat gaa
Leu Ala Leu Val Lys Gln Asn Pro Lys Val Ser Leu Ile Glu Tyr Glu
                                      10
                  5
aat tac ttt agc caa ctc aaa tac aac cct aac gca agc aag agc gat
                                                                   96
Asn Tyr Phe Ser Gln Leu Lys Tyr Asn Pro Asn Ala Ser Lys Ser Asp
                                 25
             20
att gcc ttt ttt tat gcc ccc aac caa gtc tta tgc acc acg att aca
                                                                   144
Ile Ala Phe Phe Tyr Ala Pro Asn Gln Val Leu Cys Thr Thr Ile Thr
                             40
         35
gct aaa tac ggc gcg ttg ctt aaa gaa att tta agc cag aat aaa gtc
                                                                   192
Ala Lys Tyr Gly Ala Leu Leu Lys Glu Ile Leu Ser Gln Asn Lys Val
                         55
ggc atg cat tta gcc cac agc gtg gat gtg cgt att gaa gta gcg cct
                                                                   240
Gly Met His Leu Ala His Ser Val Asp Val Arg Ile Glu Val Ala Pro
                                          75
                     70
 65
                                                                    263
aaa atc caa att aac gcc caa tc
Lys Ile Gln Ile Asn Ala Gln
                 85
<210> 134
<211> 87
<212> PRT
<213> Helicobacter pylori
<400> 134
Leu Ala Leu Val Lys Gln Asn Pro Lys Val Ser Leu Ile Glu Tyr Glu
                                      10
  1
Asn Tyr Phe Ser Gln Leu Lys Tyr Asn Pro Asn Ala Ser Lys Ser Asp
                                  25
             20
Ile Ala Phe Phe Tyr Ala Pro Asn Gln Val Leu Cys Thr Thr Ile Thr
                              40
Ala Lys Tyr Gly Ala Leu Leu Lys Glu Ile Leu Ser Gln Asn Lys Val
                                              60
                         55
Gly Met His Leu Ala His Ser Val Asp Val Arg Ile Glu Val Ala Pro
                                          75
                     70
Lys Ile Gln Ile Asn Ala Gln
                 85
<210> 135
<211> 447
<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(447)
<400> 135
ago tat goo aaa oto ato gog caa aco ato tog cat gtg ott aat ggo
                                                                    48
Ser Tyr Ala Lys Leu Ile Ala Gln Thr Ile Ser His Val Leu Asn Gly
                                      10
gga tcg ctg ttg gtg agc gcg gat tct tct agg cac tgg ttt tta aac
                                                                    96
Gly Ser Leu Leu Val Ser Ala Asp Ser Ser Arg His Trp Phe Leu Asn
                                  25
tac att ctt tct aac cta aac ccc aaa gat tta aaa gag cgc ccc tta
Tyr Ile Leu Ser Asn Leu Asn Pro Lys Asp Leu Lys Glu Arg Pro Leu
                              40
ttg tcc gtc att gat ttt aac gct tct tct ttc tac ccc aaa aac gat
Leu Ser Val Ile Asp Phe Asn Ala Ser Ser Phe Tyr Pro Lys Asn Asp
                          55
      50
```

```
gcg aat ctc tct cta gcc acc ata gag atg act tat caa aac ccc atg
                                                                   240
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Phe Trp His Val Gly Lys Ile Glu Asn Glu Gly Leu Lys Thr Ile Leu
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Leu Ser Lys Ile Pro Ser Phe Leu Trp Leu Phe Glu Glu Leu Lys Glu
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Asp Cys Leu Leu Leu Lys Glu His Asp Ser Leu Leu Asp Tyr Lys Leu
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Lys Tyr Glu Gly Glu Gly Val Phe Leu Asp Gln Glu Asn Lys Ile Leu
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Tyr Ala Gly Val Lys Glu Asp Asp Val His Leu Leu Arg Glu Ser Ala
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Cys Leu Ala Val Arg Thr Leu Lys Lys Leu Ala Phe Lys Ser Val Lys
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gtg ggc gtt tat act tgt ggt gca cat tct aaa gat aac gcg ctt tta
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Val Gly Val Tyr Thr Cys Gly Ala His Ser Lys Asp Asn Ala Leu Leu
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Glu Asn Leu Lys Ala Leu Phe Leu Gly Leu Lys Leu Gly Leu Tyr Glu
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Tyr Asp Thr Phe Lys Ser Asn Lys Lys Glu Ser Val Leu Lys Glu Ala
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Ile Val Ala Leu Glu Leu His Lys Pro Cys Glu Lys Thr Cys Ala Asn
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Ser Leu Glu Lys Ser Ala Lys Glu Ala Leu Lys Tyr Ala Glu Ile Met
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Thr Glu Ser Leu Asn Ile Val Lys Asp Leu Val Asn Thr Pro Pro Met
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Ile Gly Thr Pro Val Tyr Met Ala Glu Val Ala Gln Lys Val Ala Lys
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Glu Asn His Leu Glu Ile His Val His Asp Glu Lys Phe Leu Glu Glu
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Lys Lys Met Asn Ala Phe Leu Ala Val Asn Lys Ala Ser Leu Ser Val
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ttg	agc Ser	ttg	add	Des	NI n) an	Tur	Met	Val	Thr	Met	Lvs	Ala	Asp	Lvs	
Leu	Ser	Leu		PIO	VIG	vah	1 1 1	265	141	1114		-,,-	270		-1-	
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Dho	Thr	Ser	Ala	Tle	Met	Glv	His	Asn	Ğlu	Glu	Leu	Lys	Asn	Leu	Phe	
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Asn	Arg	UIS	Tien	405	шyз	шси			410	-,-			•	415	-	
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aat	Ile	Cor	Cor	Cor	Ara	Tur	Glv	Glv	Ala	Tle	Thr	Ala	ĞÎv	Leu	Phe	
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Glu	Leu	Leu	Lys		Ala											
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Lvs	Tvr	Glu	Gly	Glu	Gly	Val	Phe	Leu	Asp	Gln	Glu	Asn	Lys	Ile	Leu	
-,,	- 2 -	35	•		-		40					45				

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Ala	Ala	Lys · 35	Ser	His	Lys	ĞÎÿ	Gln 40	Tyr	Arg	Lys	Ser	Gly 45	Glu	Pro	Tyr	
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                            120
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145					130				~~~		202	aac	agt	caa	taa	528
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Asn	Ala	Asp		ASP	гуэ	GIU	цуз	105	014				190			
			180					185						++-	330	624
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712	Aen	Len	Thr	Leu	Leu	Lys	Arg	Lys	Lys	Asn	Ala	His	Ala	Leu	Asn	
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Glu Glu Lys Arg Leu Leu Glu Gln Ile Gln Thr Lys His Phe Lys Glu
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Arg Glu Ile Gly Val Pro Ala Ile Val Gly Val Ser Gly Ala Thr Asp
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gag ggc tat gtg tat gcg ggc att tat gag cat gaa att gaa agg gtg
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Val Gly Leu Ala Arg Met Glu Met Ile Ile Leu Asn Gln Ile Lys Ala
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                             40
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Thr Leu Asn Lys Asn Gln Asn Thr Asp Tyr Val Phe Thr Cys Ser Pro
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Phe Ser Ala Ser Pro Tyr Arg Ser Phe Ser Leu Glu Asn Gly Val Gln
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                                         75
Met Ala Phe Lys Glu His Ser Asn Thr Arg Thr Gln Asp Leu Lys Thr
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                 85
Leu Tyr His Asp Ala Gly Leu Leu Tyr Met Gly Lys Ala Gln Ala Phe
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                                                     110
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Lys Glu Met Arg Pro Ile Phe Ser Gln Asn Ser Ile Ala Leu Glu Leu
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Leu Tyr Glu Lys Ser Asp Gly Pro Thr Leu Lys Ser Phe Asp Gln Phe
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Asp Thr Glu Ser Gly Lys Ile Gln Ile Phe Ser Gln Lys Cys Ala Asp
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Phe Lys Leu Ala Asp Phe Lys Gly His Pro Thr . Trp Phe Glu Pro Ala
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Glu Trp Leu Gly Ser Lys Met Ala Glu Ile Tyr Pro Phe His Leu Ile
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Ser Pro His Pro Lys Tyr Arg Val Asn Ser Gln Leu Asp Asn Thr Trp
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 Gly Tyr Met Leu Ile Val Trp Asp Phe Ile Arg Tyr Ala Lys Glu Met
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 Gly Ile Pro Val Gly Pro Gly Arg Gly Ser Ala Ala Gly Ser Leu Val
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 Ala Phe Ala Leu Lys Ile Thr Asp Ile Asp Pro Leu Lys Tyr Asp Leu
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Val Leu Asp Leu Lys Asn Ser Gln Leu Val Phe Gly Asp Gln Gly Ser
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 Ala Lys Asn Gln Thr Tyr Ser Phe Thr Asn Pro Leu Asn Asn Ala Leu
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Lys	Ala	Ser 35	Ser	Thr	Val	Leu	Thr 40	Leu	Gln	Ala	Ser	45	СТĀ	TTE	THE	
адс	aσt	222	aat	gcg	gaa	att	tct	ctt	tat	gat	ggc	gcc	acg	ctc	aat	192
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Pro 145	Pro	GIU	GIĀ	GLY	150	Lys	vob	цуз		155		-7-	•		160	
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Thr	Thr	Gln	Asn	Asn 165	Ala	Asn	Asn	Asn	Gln 170	Gln	Asn	Ser	ATa	175	· Asn	
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Ile	Asn .370	Glu	Leu	Val	Val	Lys 375	Thr	Asn	Gly	Val	Ser 380	Val	Gly	Glu	Tyr	
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Asn	Tyr	Phe 435	Asp	Ala	Arg	Asn	11e 440	ГÀघ	Asn	Val	Glu	11e 445	Thr	Arg	Lys	
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Phe	Ala 450	Ser	Ser	Thr	Pro	Glu 455	Asn	Pro	Trp	Gly	Thr 460	Ser	Lys	Leu	Met	
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Pho	Asn	Asn	Leu	Thr	Leu	Glv	Gln	Asn	Ala	Val	Met	Asp	Tyr	Ser	Gln	
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Dha	Cor	Aen	Len	Thr	Tle	Gln	Clv	Asp	Phe	Ile	Asn	Asn	Gln	ĞÎy	Thr	
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aat	gcg	gca	gct	atg	TTC	בכנ	agt	aat	aat	grg	gat	age	gcg	act	999	1304
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	Lys	•														
	0> 1	36														
	1> 5															
	2> PI															
			obact	-07 1	וח לער	ri										
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65 Leu	Gln	Tyr	Val		70 Ala	Tyr	Leu	Ala	Pro	75 Ser	Tyr	Ser	Thr	Ile 95	
Thr	Ser	Lys		85 Thr	Gly	Glu	Val	Asn 105	90 Phe	Asn	His	Leu	Thr		Gly
Asp	His		100 Ala	Ala	Gln	Ala	Gly 120	Ile	Ile	Ala	Ser	Asn 125		Thr	His
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					วรก			Ser Asn		233					240
				245				Thr	230						
_			260					265					210		Ser
		275					280				Thr	203			Thr
	200					295				Arg	300				Lys 320
200				Thr	310 Ala					Ile					Gly
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		255	Ile	Thr			360	Asn	Val			203			Asn
	~=~	Glu	Leu			275					200				Tyr
205					390	1				ンフィ					Val 400
_				405					410					415	
_			420	١				425)				400		Trp Lys
		436	:				441	,				773	•		Met
	AEC	١				455	Ď				400	,			Gln
4.00					476					4/3)			Gly	Thr
				489	5				490	,			Asn	Val	Gly
			500	1			e Sei	505 Asr)			Ser	Ala	'	Gly
	∍ Tyı	519 Gl:	5			Lys	520 11e)				Asp	,		. Lys
Asr 545) ₃ Glı	ı His	s Vai	L Let 550	539 Let)	ı Ly:	a Ala	Lys	555	Ile	Gly	Tyr	Gly	Asn 560

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35	aac ccg gtt Asn Pro Val	Tyr Ile Gly	Gln Ile Ile	Gly Val Thi	Tyr							
Asp Leu Leu	Leu Phe Asp	gct gag ttt Ala Glu Phe 55	Leu Glu Ala 60	Lys Ile Lys	s Asp							
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aaa aag gtg Lys Lys Val	Glu Lys Glu 85		Ala Thr Tyr 90	Tyr Tyr Lys	i lle							
Lys Gly Ile	Lys Ala Ile 100	att ccg tcc Ile Pro Ser 105	Leu Glu Val	Ser Ala Pho	e Ser							
Asn Lys Asp 115	Lys Tyr Ile	gat cat tcc Asp His Ser 120	Ile Ala Pro	Lys Val Thi	r Leu							
Gln Val Thr	Asp Leu Ser	aaa aac cct Lys Asn Pro 135	Arg Tyr Ala 140	Asn Val Me	t Ala							
Lys Asp Leu	Gln Val Leu 150	caa tac aaa Gln Tyr Lys	Thr Lys Asp 155	Tyr Asp As	160							
Asn Asn Ile	Leu Val Met	gaa ata gcg Glu Ile Ala	Phe Lys Glu 170	Ala Thr Tr	e GIn							
Asp Phe His	Ile Lys Glu 180	gcg atc aag Ala Ile Lys 185	Gln Gly Phe	Asp Asn Ala	a Ser							
Leu Asn Gln 195	Ile Lys Ala	aaa gaa ggg Lys Glu Gly 200	Ser Val Phe	Tyr Tyr Cy	s vai							
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Asp Leu Leu Phe Asp Ala Glu Phe Leu Glu Ala Lys Ile Lys Asp
Gly Leu Asp Lys Thr Gln Ile Glu Leu Leu Asn Lys Met Pro Lys Trp
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Lys Lys Val Glu Lys Glu Leu Phe Arg Ala Thr Tyr Tyr Lys Ile
                 85
Lys Gly Ile Lys Ala Ile Ile Pro Ser Leu Glu Val Ser Ala Phe Ser
                                                    110
Asn Lys Asp Lys Tyr Ile Asp His Ser Ile Ala Pro Lys Val Thr Leu
                                                125
                            120
        115
Gln Val Thr Asp Leu Ser Lys Asn Pro Arg Tyr Ala Asn Val Met Ala
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                                            140
Lys Asp Leu Gln Val Leu Gln Tyr Lys Thr Lys Asp Tyr Asp Asp Lys
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145
Asn Asn Ile Leu Val Met Glu Ile Ala Phe Lys Glu Ala Thr Trp Glu
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Asp Phe His Ile Lys Glu Ala Ile Lys Gln Gly Phe Asp Asn Ala Ser
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                                185
Leu Asn Gln Ile Lys Ala Lys Glu Gly Ser Val Phe Tyr Tyr Cys Val
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att gag ctt tcc acc gtg aat tat tta gcc cct tta att ttc aat ttg
Ile Glu Leu Ser Thr Val Asn Tyr Leu Ala Pro Leu Ile Phe Asn Leu
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gac aag cag ctc atg ggg caa gtg gtt ttg gat tct aac aaa tac cca
Asp Lys Gln Leu Met Gly Gln Val Val Leu Asp Ser Asn Lys Tyr Pro
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cac tac cat tta aga gag aat att cta agc cac acg cat gaa
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His Tyr His Leu Arg Glu Asn Ile Leu Ser His Thr His Glu
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1	ttc	2+0	tat	5	atc	agc	gag	ttc		aaa	qcc	tat	acc		ttg	96
Gly	Phe	Ile	Tyr 20	Glu	Ile	Ser	Glu	Phe 25	Met	Lys	Ala	Tyr	30	ATG	rea	
cta	aaa	aaa	caa	gac	cga	tac	gtc	tat	tta	ttg	agg	tat	ctc	CCC	tct	144
Leu	Lys	Lys 35	Gln	Asp	Arg	Tyr	Val 40	Tyr	Leu	Leu	Arg	Tyr 45	Leu	Pro	ser	192
agg	tat	tgg	gcc	agc	att	tta	acg	act	gcc Ala	T.A.I	Tur	Val	Lvs	Tvr	Pro	132
_	Tyr 50					55					60					240
gat	ttt Phe	gac	gct	LEG	T.ve	Lvs	Len	Leu	Val	Ser	Tvr	Tyr	Tyr	Gln	Thr	
65					70					75					80	
+ 00	att Ile	gca Ala	gga Gly	ggc Gly 85	acg Thr	atc Ile	acg Thr	cgc Arg	atc Ile 90	aag Lys	caa Gln	acc	agt Ser	atc Ile 95	aac Asn	288
att	atc	aaa	aac	att	aaa	agc	aat	aag	agc	gtt	gaa	acc	atc	aaa	gag	336
Ile	Ile	Lys	Asn 100	Val	Lys	Ser	Asn	Lys 105	Ser	Val	Glu	Thr	11e	гÃ2	GIU	
ctt	ata	ttg	aat	agc	atc	gac	tct	tat	aac	acc	ttt	gat	caa	tac	ctc	384
Leu	Ile	Leu 115	Asn	Ser	Ile	Asp	Ser 120	Tyr	Asn	Thr	Phe	125	GIN	Tyr	rea	432
tat	aac Asn	tta	tgg	gat	agc	tct	tct	gtt	Tur	Cat	Ser	aaa I.vs	Tro	Val	Ara	432
_	Asn 130 gtc					135					140					480
CCT	gtc Val	LEA	Ala	Leu	Ala	Asn	Tvr	Phe	Met	Ala	Asp	Glu	Glu	Lys	Pro	
1 4 5					150					155					TOO	
	+++	atc	gct	atg	gat	gcc	gaa	acc	caa	gtg	gag	cat	att	ttg	cca	528
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caa	acg	CCC	aaa	aga	ggc	agt	Caa	Trn	Asn	Ala	Asp	Phe	Asp	Lvs	gaa Glu	0.0
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aaa	aga	gaa	gaa	tgg	gta	aat	aat	atc	gcg	aat	Len	Thr	Leu	Len	aag · Lvs	024
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Arg	Lys 210	Lys	Asn	Ala	His	Ala 215	Leu	Asn	Gly	Asp	220	Asp	GIU	гÀг	Arg	720
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225				++~	230	age	aat	tat	agg			aat	gag	aag	tcc	768
ato	: act	T.vs	Glu	Leu	Tvr	Ser	Asn	Tyr	Arg	Lys	Trp	Asn	Ğlu	Lys	Ser	
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cto	caa	gag	cga	tac	aaa	tct	ttg	tat	aac	act	atc	acg	cct	gtt	tta	816
Lev	Gln	Glu	Arg	Tyr	Lys	Ser	Leu	Tyr 265	Asn	Thr	TIE	Thr	270	vai	Ten	864
cac	ata	gag	ggg	caa	gaa	gat	gat	ttt	gaa	gat	gat	CCC Dha	gat	cta e.i	gaa Glu	004
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Arg Tyr Trp Ala Ser Ile Leu Thr Thr Ala Leu Tyr Val Lys Tyr Pro
Asp Phe Asp Ala Leu Lys Lys Leu Leu Val Ser Tyr Tyr Tyr Gln .Thr
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Trp Ile Ala Gly Gly Thr Ile Thr Arg Ile Lys Gln Thr Ser Ile Asn
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Ile Ile Lys Asn Val Lys Ser Asn Lys Ser Val Glu Thr Ile Lys Glu
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Leu Ile Leu Asn Ser Ile Asp Ser Tyr Asn Thr Phe Asp Gln Tyr Leu
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Tyr Asn Leu Trp Asp Ser Ser Ser Val Tyr His Ser Lys Trp Val Arg
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Pro Val Leu Ala Leu Ala Asn Tyr Phe Met Ala Asp Glu Glu Lys Pro
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His Phe Ile Ala Met Asp Ala Glu Thr Gln Val Glu His Ile Leu Pro
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Gln Thr Pro Lys Arg Gly Ser Gln Trp Asn Ala Asp Phe Asp Lys Glu
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Lys Arg Glu Glu Trp Val Asn Asn Ile Ala Asn Leu Thr Leu Leu Lys
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Arg Lys Lys Asn Ala His Ala Leu Asn Gly Asp Phe Asp Glu Lys Arg
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Lys Ile Tyr Gly Gly Lys Asp Thr Ser Lys Val Ile Ser Cys Tyr Asp
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Ile Thr Lys Glu Leu Tyr Ser Asn Tyr Arg Lys Trp Asn Glu Lys Ser
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Leu Gln Glu Arg Tyr Lys Ser Leu Tyr Asn Thr Ile Thr Pro Val Leu
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tca cgc aaa aat agg gcg cga aat ttt atg cca aga atg cca aaa gat
                                                                   96
Ser Arg Lys Asn Arg Ala Arg Asn Phe Met Pro Arg Met Pro Lys Asp
                                 25
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tcg cac tcg caa ggc ttt gag act tta agc att aat ttt gaa ggc acg
                                                                   144
Ser His Ser Gln Gly Phe Glu Thr Leu Ser Ile Asn Phe Glu Gly Thr
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Gly Phe Leu Val Ser Ile Asn Gly Val Met His Val Ile Tyr Pro Pro
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 Lys Glu Ser Ala Leu Glu Tyr Leu Lys Ala Asn Leu Ser Ser Gln Phe
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Gly	Gly	Tyr	Glu	Gly	Val	Asn	Trp	Gly 25	Lys	Thr	Gly	Tyr	Ile 30	Thr	GIÀ	
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Asn	Gly	Ala	Gln	Thr	Gly	GTÄ	Gly	Ala	Thr	Leu	Asn 60	Pne	vaı	GTÅ	MIG	
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act	gaa	Ile	aat	atc	D) a	Glu	Ala	Thr	Phe	Lvs	Asn	Leu	Lys	Thr	Thr	
	Glu	TTE	Asn	116	70	GIY	MIG	****	- 110	75			-,		80	
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Gly	Gly	Tyr	Asp	Phe	Thr	GIY	Asn	GIĀ	vaı	Pne	Asp	125	Val	non	1110	
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aac	aag	gct Ala	Tac	Tur	T.vs	Phe	Gln	Glv	Thr	Glu	Asn	Ser	Tyr	Asn	Phe	
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Thr	Ile	Glu	Lys		Val	Leu	Ser	Asp	A1a 170	Ser	Tyr	THE	FIIE	175	GLY	
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acg	aat	aac Asn	acc	ממט	The	Glu	yac Asn	Lus	Phe	Asn	Asn	Glv	Ser	Phe	Asn	
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Gly	Let	Leu	Ser	Ser	Leu	Ser	val	GTA	Inr	inf	ıyı	285	. nec		Asn	
		275			4		280	ځوو	220	act	tto			ato	ctg	912
gct	aaa	ago	gtg	gat	tat	aag	yat	aal Den	Den	Ala	J.en	Tur	Glr	Met	Leu	
Ala			val	Asp	TAL	дуя 295	nap	noil	ا د حيو .		300					
	290	++	24+	aaa	กลล	aac	cct	aσc	gac	aca	cta	gta	aat	aac	gat	960
cgt	. rgg	, all	Ser	Glu	Glu	Asn	Pro	Ser	Gly	Thr	Leu	Val	Asr	Lys	Asp	
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305					310					315					320	

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Gln :	Ser	Ala	Pro	Asn	Ser	Ala	ГÀ2	Tre	330	ASII	AGI			335		
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Th.≠	Dha	Thr	20 Ala	Asp	Arg	Val	Tyr	Ile	Thr	Gly	Asn	Met	Met	Thr	Gly	
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Car	בות	Lve	Tle	85 Asn	Val	Ser	Gln	Ser	Asp	Phe	Tyr	Asp	Trp	Thr	Gly	
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145	Tle	. Glu	1.05	Ser	150 [Va]	Let	Ser	Asp	Ala			Thr	Phe	Asp	Gly	
Thr	Asr	a Asr	Thr	Phe	Thi	Gli	ı Asp	Lys 185	Phe	Asn	ASD	СТА	190)	Asn	
5 1	0		180 - וג) . (2):	ı Glr	Th:	. Ast	Ala	Phe	Asr	. Asn	Asn			Asn	
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Gly	Gly	/ Sei	Phe	Se	r Phe	Ası	n Ala	Lys	Glr	ı Val	220	Pne	Se i	. GIA	Asn	
	210)		. (1)	. Va	21:	o Asr	n Phe	Ası	n Asr	Thr	Pro	Lys	, Val	Ser 240	
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Phe	Th	r Ası	Ası	Th	r Pho	e Ası	n Val	L Asr	Ası	n Gli	n Phe	Lys	; Ile	255 e	Gly	
				241	5				ZJI	J					Gln	
			261	^				Zb:)				2,,,	•		
Glv	, Le	u Le	ı Se:	r Se	r Le	u Se	r Vai	l Gly	Th	r Th	г Туз	: Glr	ı Le	ı Let	ı Asn	
		071	-				2X1	1				20,	,			
	~ ~	^					~				JU.	,			t Leu	
Arc	29 Tr	o D Il	e Se	r Gl	y Gl	u As	n Pro	o Sei	G1;	y Th	r Le	ı Val	l As	n Ly:	320	
	_				21	n				21.	J					
Glr	ı Se	r Al	a Pr	o As 32	n Se	r Al	a Ly	s Ile	33; 33;	r asi	ıı va.	. ni	. III	33	r Asp 5	
N	ري م	v T.e	u Th	32 r Tv	o r Tv	r Il	e Ly	s Gl	ı Ası	n Ph	e Ası	n Ası	n Gl	y Ile	e Thr	
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Ser Leu Val Lys Gly Leu Lys Glu Arg Glu Ile Leu Asp Leu Ile Ala
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                            120
caa aaa tat caa atc att gag gca gaa aaa ccc aaa caa ggg tct tct
                                                                    432
Gln Lys Tyr Gln Ile Ile Glu Ala Glu Lys Pro Lys Gln Gly Ser Ser
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cat age gat gat ttt tgc caa tet tgc aat egt ate egt ttg get tet
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 Ala Ile Arg Ile Lys Gly Ile Ala Arg Glu His Asp Ile Glu Ile Ile
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          . 100
 gaa aat aaa acg ctc gcc aga gag ctt tat aga gat gtg aaa tta aac
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Leu Lys Asn Ala Thr Asn Lys Met Met Gln Glu Ile Pro Lys Ala Asn
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Val Val Val Thr Asn Pro Thr His Tyr Ala Val Ala Leu Lys Phe Asp
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Glu Glu His Pro Val Pro Val Val Val Ala Lys Gly Thr Asp Tyr Leu
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Ala Ile Arg Ile Lys Gly Ile Ala Arg Glu His Asp Ile Glu Ile Ile
                                                     110
                                105
            100
Glu Asn Lys Thr Leu Ala Arg Glu Leu Tyr Arg Asp Val Lys Leu Asn
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        115
Ala Ala Ile Pro Glu Glu Leu Phe Glu Ala Val Ala Ile Val Phe Ala
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ccc att ata ggc gat acg ctt tat aat aac gag cca agt tta gcc aaa
Pro Ile Ile Gly Asp Thr Leu Tyr Asn Asn Glu Pro Ser Leu Ala Lys
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cgc ttg atg ctc cat gca cat aaa atc gcg cta cta ggg tat gaa ttt
Arg Leu Met Leu His Ala His Lys Ile Ala Leu Leu Gly Tyr Glu Phe
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gaa gcg atc gct cct aaa gaa ttt gaa att
Glu Ala Ile Ala Pro Lys Glu Phe Glu Ile
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Glu Ala Ile Ala Pro Lys Glu Phe Glu Ile
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Gln Glu Met His Ile Leu Met Ile His Ile Leu Cys Asp Cys Ile Glu
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agg cat ttc gct cat aaa aat
Arg His Phe Ala His Lys Asn
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<213> Helicobacter pylori
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Gln Glu Met His Ile Leu Met Ile His Ile Leu Cys Asp Cys Ile Glu
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Arg His Phe Ala His Lys Asn
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Arg His Tyr Glu Thr Met Phe Ile Leu Lys Pro Thr Leu Val Glu Glu
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 gag att aaa tcc aag att gag ttt tat aaa gaa gtg atc act aag cat
                                                                    96
 Glu Ile Lys Ser Lys Ile Glu Phe Tyr Lys Glu Val Ile Thr Lys His
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 cac ggc gtg att gaa acg agc ctg gat atg ggc atg cgt aat tta gct
 His Gly Val Ile Glu Thr Ser Leu Asp Met Gly Met Arg Asn Leu Ala
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 tat gaa atc aaa aag cac aaa aga ggc tat tat tat gtg gcg tat ttc
                                                                    192
 Tyr Glu Ile Lys Lys His Lys Arg Gly Tyr Tyr Tyr Val Ala Tyr Phe
                          55
 aaa gcg gag ccg tca atg att gta gag ctt gaa cga ttg tat cgc atc
                                                                    240
 Lys Ala Glu Pro Ser Met Ile Val Glu Leu Glu Arg Leu Tyr Arg Ile
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                      70
  65
 aat gaa gac gtg ttg cgt ttc att gtg atc aaa tac gaa agc aag aaa
                                                                    288
 Asn Glu Asp Val Leu Arg Phe Ile Val Ile Lys Tyr Glu Ser Lys Lys
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 gaa gtg gaa gcg tgg cat gcg ttg gtg gat agg gct aat aaa aag cca
 Glu Val Glu Ala Trp His Ala Leu Val Asp Arg Ala Asn Lys Lys Pro
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             100
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tcg cac gcc aaa gaa aaa cac gaa aaa acc gaa cac acg cat tct cac
Ser His Ala Lys Glu Lys His Glu Lys Thr Glu His Thr His Ser His
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cac aca gag gaa gca gaa agc gta gga tct cat agc gaa
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Tyr Glu Ile Lys Lys His Lys Arg Gly Tyr Tyr Tyr Val Ala Tyr Phe
                         55
Lys Ala Glu Pro Ser Met Ile Val Glu Leu Glu Arg Leu Tyr Arg Ile
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 65
Asn Glu Asp Val Leu Arg Phe Ile Val Ile Lys Tyr Glu Ser Lys Lys
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Glu Val Glu Ala Trp His Ala Leu Val Asp Arg Ala Asn Lys Lys Pro
                                                     110
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                  5
atg agc gct gaa gaa gtg gaa gca gag att gaa cgg ctg ctg aac aaa
                                                                    96
Met Ser Ala Glu Glu Val Glu Ala Glu Ile Glu Arg Leu Leu Asn Lys
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cgc caa gaa gcc gat aaa gaa cga aga gct caa aaa aaa caa gaa gcc
Arg Gln Glu Ala Asp Lys Glu Arg Arg Ala Gln Lys Lys Gln Glu Ala
                                                  45
                              40
         35
aaa ccc aaa caa gaa gtt acc cca aca aaa gaa acc ccc aaa gcc cct
                                                                    192
Lys Pro Lys Gln Glu Val Thr Pro Thr Lys Glu Thr Pro Lys Ala Pro
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 aaa acc gaa act aaa gct aa
 Lys Thr Glu Thr Lys Ala
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Ser Ser Asp Asn Pro Leu Ala Asp Glu Pro Asp Leu Asp Tyr Ala Asn
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Met Ser Ala Glu Glu Val Glu Ala Glu Ile Glu Arg Leu Leu Asn Lys
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              20
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Arg	Gln	Glu	Ala	Asp	Lys	Glu		Arg	Ala	Gln	Lys	Lys	Gln	Glu	Ala	
Lys	Pro	35 Lys	Gln	Glu	Val	Thr	40 Pro	Thr	Lys	Glu	Thr	Pro	Lys	Ala	Pro	
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Lys 65	Thr	Glu	Thr	Lys	70											
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	.> 79 !> DN															
			bact	er p	ylor	i										
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Ala	Glu	Glu	Ser	Lys	Gly	Ser	Val	Ala	гÀг	Tyr	Lys	Ile	Glu	LTO	Gln	
· 1				5					10					13		96
tac	agc	att	gat	ttt Phe	gat	Ser	gca	Glu	His	Thr	Ser	Leu	Phe	Ile	Pro	,
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Met	Pro	Ser	Val	Val	Ala	Ser	Asn	Val	His	Leu	Gln	Gly 45	Asn	His	ATA	
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	Leu	Lys	Ser	Thr		Lys	Lys	Gin	Vai	н18 75	ren	Ser	TÀT	GIU	80	*
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gct Ala	Ser	Tvr	Gln	Leu	Asn	Glu	Arg	Leu	Phe	Ğlu	Thr	Ser	Asp	FILE	Val	
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gca	atg	ggg	cgt	tat	gaa	aga	gac	gat	gcg	agc	gtg	gct Ala	aac Asn	Ile	Ala	330
Ala	Met	Gly	Arg 100	Tyr	GIU	Arg	Asp	105	WIG	261	Val	ALC.	110			
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Asn	Gln	Leu	Lys	Gly	Thr	Thr	Pro	Lys	Glu	Ser	Val	Arg	Asn	Phe	Tyr	
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gcg	ttc	atc	aag	cat	gag	atg	CCT	aag Lvs	aga	Gln	Lvs	Ala	Leu	Glu	Gly	
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Lys	Glu	Asn	Leu	Pro	Lys	Arg	Glu	Ser	Leu	Pro	Trp	Phe	Ala	Thr	Ile 160	
9 4 5					150					TOO					100	528
tca	aaa	gag	agc	atg Met	Dhe	gcg Val	Ser	Leu	Cvs	His	Ala	Cys	Gly	Ile	aaa Lys	
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Ser	Ala	Ğlu	Val	Gln	Gly	Leu	Lys	Leu	GTA	Gln	Asn	Ser	190	Val	Lys	
			180			-+-	+ = +	185		gat	tca	ttt			ttt	624
aac	gct	CCT	aga	gtg Val	Glu	Val	Tvr	Leu	Lvs	Asp	Ser	Phe	Leu	Ala	Phe	
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Āsp	Phe	Gln	Asn	Asn	His	Lys	Glu	Val	Phe	Ile	Pro	Leu	Asn	Arg	His	
	210			L L-	+	215	~~~	++=	++~	aca	220 act		gac	gat	gct	720
aaa	gac	atg	cag	נים.ו	gat	Ser	Ala	Leu	Leu	Ala	Thr	Phe	Gly	Asp	Ala	
225					230					235					240	
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Phe	Ala	Leu	Val	Asp	Gly	Arg	Asp	Leu	Gly	Asn	Tyr	Glu	Ser	ьys	Leu	

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Phe	Glu	Lys	Arg 260	Val	Ser	Tyr	Thr	Ile 265	Val							
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	!> PF !> He		bact	er r	vlor	i							•	•		
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Ala	Glu	Glu		5					10					Ala 15		٠
			20					2,5					20	Ile		
		35					40					43		His		•
	EΛ					55					υď			Val		
<i>_</i>					70					15				Glu	00	
	•			85					90					Phe 95		
			100					105					110	Ile		
		115					120					123		Phe		
	120					135					140			Glu		
. 1 4 5					150					122				Thr	100	
				165					170					11e 175		
			180					185					130	Val		
		105					200					203		Ala		
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			260		Ser	Tyr	Thr	265	Val							
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Cys	Met	: Phe	e Asp	Gly	y Tyr S	Thi	HIS	туг	тец 10	i Asii	ı nen	ı vaı	Den	15	non	00
		ata Ile	a gaç e Glu	g cto 1 Lei	tct Ser	ggt Gly	gto Val	. Arg	gaa Glu	tgo Cys	att Ile	gaa Glu	GIU	Der	gaa Glu	96
			20	`				25)				30	,		144
gg	gt	g gat	ggg	gca	gto	agt	gaa	acc	gct Ala	. agt Ser		. cat : His	Leu	. Cys	gtg	417
	•	3	5				40)	, A10			45		- 3 -		170
aaa	a gct	tti	a gc	g aaa	a ggo	CC	ı ya	יים ג								

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Lys Ala Leu Ala Lys Gly Ser Glu
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<211> 56
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Cys Met Phe Asp Gly Tyr Thr His Tyr Leu Asn Leu Val Leu Val Asn
Cys Pro Ile Glu Leu Ser Gly Val Arg Glu Cys Ile Glu Glu Ser Glu
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Lys Ala Leu Ala Lys Gly Ser Glu
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Gly Gly Ile Ala Cys Ala Asn Leu Leu His Lys Asn Ser Gly Ile Thr
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ata gat att gga ggg ggt agc acc gag tgc gcg ttg att gaa aaa ggc
                                                                   96
Ile Asp Ile Gly Gly Gly Ser Thr Glu Cys Ala Leu Ile Glu Lys Gly
                                 25
             20
aag att aag gac tta atc tcg ctt gat gtt ggg acg att cgc att aaa
Lys Ile Lys Asp Leu Ile Ser Leu Asp Val Gly Thr Ile Arg Ile Lys
                              40
         35
gaa atg ttt tta gac aaa gac tta gag gtc aaa ttg gct aaa gcc ttt
                                                                   192
Glu Met Phe Leu Asp Lys Asp Leu Glu Val Lys Leu Ala Lys Ala Phe
                                              60
                         55
atc caa aaa gaa gtc tct aaa ctg ccc ttt aaa cac aaa aac gcc ttt
                                                                    240
Ile Gln Lys Glu Val Ser Lys Leu Pro Phe Lys His Lys Asn Ala Phe
                                          75
                     70
ggg gtg ggg ggg acg atc aga gcg ttg agt aag gta ttg atg aaa cgc
                                                                    288
Gly Val Gly Gly Thr Ile Arg Ala Leu Ser Lys Val Leu Met Lys Arg
                                      90
                 85
ttt tgt tac cct att gat tct ttg cat ggc tat gaa ata gat gca cat
                                                                    336
Phe Cys Tyr Pro Ile Asp Ser Leu His Gly Tyr Glu Ile Asp Ala His
                                105
aaa aat tta gcg ttc att gaa aaa atc gtc atg ctc aaa gaa gat caa
Lys Asn Leu Ala Phe Ile Glu Lys Ile Val Met Leu Lys Glu Asp Gln
                                                 125
                            120
tta cgg ctt tta ggg gtg aat gaa gag cgt ttg gat agc atc agg agc
Leu Arg Leu Leu Gly Val Asn Glu Glu Arg Leu Asp Ser Ile Arg Ser
                         135
ggg gcg ttg att tta tca gtc gtt ttg gag cat tta aaa act tct tta
Gly Ala Leu Ile Leu Ser Val Val Leu Glu His Leu Lys Thr Ser Leu
                                         155
                    150
 atg atc act agt ggg gtg ggg gtg aga gga ggc gtg ttt ttg agc gat
                                                                    528
Met Ile Thr Ser Gly Val Gly Val Arg Glu Gly Val Phe Leu Ser Asp
                                     170
 tta ttg cgc cat cat tac cat aaa ttc ccc ccc aat atc aac ccc tct
 Leu Leu Arg His His Tyr His Lys Phe Pro Pro Asn Ile Asn Pro Ser
                                 185
             180
 ctc atc tct tta aaa gat cgc ttt ttg ccc cat gaa aag cac agc caa
 Leu Ile Ser Leu Lys Asp Arg Phe Leu Pro His Glu Lys His Ser Gln
```

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200
        195
aag gtc aaa aaa gaa tgc gtg aaa ttg ttt gaa gcc tta tcg cct ttg
Lys Val Lys Lys Glu Cys Val Lys Leu Phe Glu Ala Leu Ser Pro Leu
                        215
cat aaa ata gat gaa aaa tac ctt ttc cat tta aag att gcg ggg
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His Lys Ile Asp Glu Lys Tyr Leu Phe His Leu Lys Ile Ala Gly
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Gly Gly Ile Ala Cys Ala Asn Leu Leu His Lys Asn Ser Gly Ile Thr
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Lys Ile Lys Asp Leu Ile Ser Leu Asp Val Gly Thr Ile Arg Ile Lys
                                                 45
                              40
Glu Met Phe Leu Asp Lys Asp Leu Glu Val Lys Leu Ala Lys Ala Phe
                                             60
                         55
Ile Gln Lys Glu Val Ser Lys Leu Pro Phe Lys His Lys Asn Ala Phe
                  · 70
Gly Val Gly Gly Thr Ile Arg Ala Leu Ser Lys Val Leu Met Lys Arg
                                     90
                 85
Phe Cys Tyr Pro Ile Asp Ser Leu His Gly Tyr Glu Ile Asp Ala His
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                                105
Lys Asn Leu Ala Phe Ile Glu Lys Ile Val Met Leu Lys Glu Asp Gln
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Leu Arg Leu Leu Gly Val Asn Glu Glu Arg Leu Asp Ser Ile Arg Ser
                        135
Gly Ala Leu Ile Leu Ser Val Val Leu Glu His Leu Lys Thr Ser Leu
                                         155
                    150
Met Ile Thr Ser Gly Val Gly Val Arg Glu Gly Val Phe Leu Ser Asp
                                    170
                165
Leu Leu Arg His His Tyr His Lys Phe Pro Pro Asn Ile Asn Pro Ser
                                185
            180
Leu Ile Ser Leu Lys Asp Arg Phe Leu Pro His Glu Lys His Ser Gln
                                                 205
                             200
        195
Lys Val Lys Lys Glu Cys Val Lys Leu Phe Glu Ala Leu Ser Pro Leu
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 His Lys Ile Asp Glu Lys Tyr Leu Phe His Leu Lys Ile Ala Gly
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 atg cta gct tta ggg caa gcg cac atg aaa aag aaa gag tat gtt tta
 Met Leu Ala Leu Gly Gln Ala His Met Lys Lys Glu Tyr Val Leu
                                                      30
                                  25
 gcg tet ttt tac ttt gat gaa tac atc aag cgc ttt ggg act aag gac
                                                                   144
 Ala Ser Phe Tyr Phe Asp Glu Tyr Ile Lys Arg Phe Gly Thr Lys Asp
                             40
 aat gtg gat tat ttg act ttt tta aaa ttg caa tcg cat tat tac gct
 Asn Val Asp Tyr Leu Thr Phe Leu Lys Leu Gln Ser His Tyr Tyr Ala
```

```
60
                         55
     50
ttc aaa aac cat tct aaa gac cag gaa ttt atc tct aat tct att gtg
Phe Lys Asn His Ser Lys Asp Gln Glu Phe Ile Ser Asn Ser Ile Val
                                         75
                     70
agt tta ggc gaa ttt ata gaa aaa tac cct aac agc cgt tac cgc ccc
                                                                   288
Ser Leu Gly Glu Phe Ile Glu Lys Tyr Pro Asn Ser Arg Tyr Arg Pro
                                     90
                 85
tat gta gaa tac atg caa atc aaa ttc att tta ggg caa aat gag ctc
Tyr Val Glu Tyr Met Gln Ile Lys Phe Ile Leu Gly Gln Asn Glu Leu
            100
aat cgc gcg atc gcg aat gtc tat aaa aaa cgc cac aag cct gag ggc
                                                                   384
Asn Arg Ala Ile Ala Asn Val Tyr Lys Lys Arg His Lys Pro Glu Gly
                                                125
                            120
gtg aaa cgc tat tta gaa agg ata gat gag act tta gaa aaa gag act
                                                                   432
Val Lys Arg Tyr Leu Glu Arg Ile Asp Glu Thr Leu Glu Lys Glu Thr
                                            140
                        135
    130
aaa ccc aaa cca tcg cac atg cct tgg tat gtg tta att ttt gat tgg
Lys Pro Lys Pro Ser His Met Pro Trp Tyr Val Leu Ile Phe Asp Trp
                                        155
                    150
145
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<211> 160
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<213> Helicobacter pylori
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Ser Ser Leu Gln Ser Glu His Ile Asn Ser Pro Leu Val Pro Glu Ala
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Met Leu Ala Leu Gly Gln Ala His Met Lys Lys Glu Tyr Val Leu
                                                      30
                                 25
Ala Ser Phe Tyr Phe Asp Glu Tyr Ile Lys Arg Phe Gly Thr Lys Asp
                             40
                                                  45
Asn Val Asp Tyr Leu Thr Phe Leu Lys Leu Gln Ser His Tyr Tyr Ala
                                             60
                         55
Phe Lys Asn His Ser Lys Asp Gln Glu Phe Ile Ser Asn Ser Ile Val
                                         75
                     70
Ser Leu Gly Glu Phe Ile Glu Lys Tyr Pro Asn Ser Arg Tyr Arg Pro
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                 85
Tyr Val Glu Tyr Met Gln Ile Lys Phe Ile Leu Gly Gln Asn Glu Leu
                                                     110
                                105
            100
Asn Arg Ala Ile Ala Asn Val Tyr Lys Lys Arg His Lys Pro Glu Gly
                                                 125
                             120
        115
Val Lys Arg Tyr Leu Glu Arg Ile Asp Glu Thr Leu Glu Lys Glu Thr
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                         135
Lys Pro Lys Pro Ser His Met Pro Trp Tyr Val Leu Ile Phe Asp Trp
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 Met Lys Ala Tyr Thr Ala Leu Leu Lys Lys Gln Asp Arg Tyr Val Tyr
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 tta ttg agg tat etc ecc tet agg tat tgg gee age att tta acg act
 Leu Leu Arg Tyr Leu Pro Ser Arg Tyr Trp Ala Ser Ile Leu Thr Thr
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acc	ctt	tat	atc	222	tac	cct	gat	ttt	gac	act	tta	aaa	aag	ctt	ttg	192
Ala	Leu	Tyr	Val	Lvs	Tvr	Pro	Asp	Phe	Asp	Ala	Leu	Lys	Lys	Leu	Leu	
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Val	Ser	Tyr	Tyr	Tyr	Gln	Thr	Trp	Ile	Ala	Gly	Gly	Thr	Ile	Thr	Arg	
65					70					75					80	000
atc	aag	caa	acc	agt	atc	aac	att	atc	aaa	aac	gtt	aaa	agc	aat	aag	288
Ile	Lys	Gln	Thr		Ile	Asn	Ile	Ile	Lys	Asn	vaı	гàг	Ser	Asn 95	гÀЗ	
				85				-+-	90	225	200	atc	asc.		tat	336
agc	gtt	gaa Glu	acc	atc	aaa	gag	CEE	Tla	LLG	Agn	Ser	Tle	Agn	Ser	Tur	330
Ser	vai	GIU	100	тте	гĀ2	GIU	Ten	105	Dea	7.511	001		110		-1-	
220	200	ttt	nat	caa	tac	ctc	tat		tta	taa	gat	agc		tct	qtt	384
Acc	Thr	Phe	Asn	Gln	Tur	Leu	Tvr	Asn	Leu	Trp	Asp	Ser	Ser	Ser	Val	
Non	1111	115		· · · ·	-1-		120		-	•	•	125				
tat	cat	age	aaa	tqq	qtq	cgt	cct	gtc	tta	gcc	cta	gct	aat	tat	ttc	432
Tvr	His	Ser	Lys	Trp	Val	Arg	Pro	Val	Leu	Ala	Leu	Ala	Asn	Tyr	Phe	
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Gln	Val	Glu	His		Leu	Pro	GIN	Thr	170	гуз	ALG	GIY	Ser	175	пр	
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Ara	Lvs	Trp	Asn	Glu	Lvs	Ser	Leu	Gln	Glu	Arg	Tyr	Lys	Ser	Leu	Tyr	•
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ASP 1		nys	בעם	5	1114	0,0	,		10	•				15		•
Met	Lvs	Ala	Tyr	Thr	Ala	Leu	Leu	Lys	Lys	Gln	Asp	Arg	Tyr	Val	Tyr	
	_		20					25					30			
Leu	Leu	Arg	Tyr	Leu	Pro	Ser	Arg	Tyr	Trp	Ala	Ser	Ile	Leu	Thr	Thr	
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Ala	Leu	Tyr	Val	Lys	Tyr	Pro	Asp	Phe	Asp	Ala	Leu	Lys	Lys	Leu	Leu	
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Val	Ser	Tyr	Tyr	Tyr		Thr	Trp	Ile	Ala		GTA	Inr	TTE	Thr	Arg	
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Ile	Lys	Gln	Thr		ITe	Asn	TTE	TTE		MSI)	AGT	тАа	Jer	95	nys	
	17-7	Glu	መሎ	85	T	C1	Low	Tle	90 Leu	Agn	Ser	De	Asn		Tvr	
Ser	val	GIU	100	TTG	րձո	GIU	neu	105	Tie a	11011		-20	110		-1-	
			100													

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Asn Thr Phe Asp Gln Tyr Leu Tyr Asn Leu Trp Asp Ser Ser Ser Val
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Tyr His Ser Lys Trp Val Arg Pro Val Leu Ala Leu Ala Asn Tyr Phe
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Met Ala Asp Glu Glu Lys Pro His Phe Ile Ala Met Asp Ala Glu Thr
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Gln Val Glu His Ile Leu Pro Gln Thr Pro Lys Arg Gly Ser Gln Trp
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Asn Ala Asp Phe Asp Lys Glu Lys Arg Glu Glu Trp Val Asn Asn Ile
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Ala Asn Leu Thr Leu Leu Lys Arg Lys Lys Asn Ala His Ala Leu Asn
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Gly Asp Phe Asp Glu Lys Arg Lys Ile Tyr Gly Gly Lys Asp Thr Ser
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Lys Val Ile Ser Cys Tyr Asp Ile Thr Lys Glu Leu Tyr Ser Asn Tyr
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                    230
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Leu Tyr Gly Tyr His Leu Ala Lys Glu His Ile Tyr Lys Gln Lys Gln
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gtc att gta aca gag ggg tat ttg gat gtg att tta ttg cac cag gcg
Val Ile Val Thr Glu Gly Tyr Leu Asp Val Ile Leu Leu His Gln Ala
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Gly Phe Lys Asn Ala Ile Ala Thr Leu Gly Thr Ala Leu Thr Pro Ser
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cat ttg ccc ttg ctt aaa aaa ggc gat ccc gaa atc ctt ttg agc tat
His Leu Pro Leu Leu Lys Lys Gly Asp Pro Glu Ile Leu Leu Ser Tyr
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gat ggg gat aag gca ggg cga aac gca gcc tat aaa gcg agc ttg atg
                                                                   288
Asp Gly Asp Lys Ala Gly Arg Asn Ala Ala Tyr Lys Ala Ser Leu Met
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                 85
ttg gct aaa gag caa agg agg gga ggg gtg att ttg ttt gaa aac aac
                                                                   336
Leu Ala Lys Glu Gln Arg Arg Gly Gly Val Ile Leu Phe Glu Asn Asn
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            100
ctg gat cca gcg gat atg atc gct aat ggc cag att gaa acc tta aaa
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Leu Asp Pro Ala Asp Met Ile Ala Asn Gly Gln Ile Glu Thr Leu Lys
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                            120
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Asn Trp Leu Ser His Pro Met Ala Phe Ile Glu Phe Val Leu Arg Arg
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                        135
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Met Ala Asp Ser Tyr Leu Leu Asp Asp Pro Leu Glu Lys Asp Lys Ala
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ctt aaa gaa atg tta ggg ttt tta aaa aac ttt tcc ttg ctt tta caa
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Leu Lys Glu Met Leu Gly Phe Leu Lys Asn Phe Ser Leu Leu Gln
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Ser Glu Tyr Lys Pro Leu Ile Ala Thr Leu Leu Gln Ala Pro Leu His
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gtt tta ggg att aga gag cga gtc tct ttt cag cct ttt tac ccc aaa
Val Leu Gly Ile Arg Glu Arg Val Ser Phe Gln Pro Phe Tyr Pro Lys
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His Leu Pro Leu Leu Lys Lys Gly Asp Pro Glu Ile Leu Leu Ser Tyr
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                                         75
Asp Gly Asp Lys Ala Gly Arg Asn Ala Ala Tyr Lys Ala Ser Leu Met
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                                     90
Leu Ala Lys Glu Gln Arg Arg Gly Gly Val Ile Leu Phe Glu Asn Asn
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            100
Leu Asp Pro Ala Asp Met Ile Ala Asn Gly Gln Ile Glu Thr Leu Lys
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Asn Trp Leu Ser His Pro Met Ala Phe Ile Glu Phe Val Leu Arg Arg
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Met Ala Asp Ser Tyr Leu Leu Asp Asp Pro Leu Glu Lys Asp Lys Ala
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Leu Lys Glu Met Leu Gly Phe Leu Lys Asn Phe Ser Leu Leu Leu Gln
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                165
Ser Glu Tyr Lys Pro Leu Ile Ala Thr Leu Leu Gln Ala Pro Leu His
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Val Leu Gly Ile Arg Glu Arg Val Ser Phe Gln Pro Phe Tyr Pro Lys
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cac cat gcc cac ttt tta gcg agc gtc tta gac gca ttg tta caa gat
His His Ala His Phe Leu Ala Ser Val Leu Asp Ala Leu Leu Gln Asp
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             20
ccg cat tta aat cac ccc ttt ata ggc att gtc tgg gat ggg agt ggg
Pro His Leu Asn His Pro Phe Ile Gly Ile Val Trp Asp Gly Ser Gly
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         35
gct tat gaa aat aag att tat ggg gcg gag tgt ttt gtg ggg gat ttg
                                                                   192
Ala Tyr Glu Asn Lys Ile Tyr Gly Ala Glu Cys Phe Val Gly Asp Leu
```

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	Glv	Gln	Lvs	Ala	Ile	Lvs	Glu	Pro	Arg	Arg	Leu	Val	Leu	Glu	Ile	Ala	*
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	++-	aaa	cac	caa		aac	aaa	ctt	tta	aag	cac	att	caa	aaq	cat	ttt	336
	Tan	Lys	uie	Gla	Len	Aen	Lve	T.eu	Len	Lvs	Ara	Val	Gln	Lvs	His	Phe	
	rea	пåз	птэ	100	Deu	71311	233	200	105	-,,				110			
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	Gln	Ser	Ile	Ala	Thr	Asn		He	Gly	Arg	Leu		Asp	TTE	vaı	ATG	•
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	Phe	Ser	Leu	Asp	Leu	Thr	Gly	Thr	Ile	Ser	Phe	Glu	Ala	Glu	Ser	Gly	
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	Gln	Val	Leu	Glu	Asn	Leu	Ala	Leu	Gln	Ser	Asp	Glu	Ile	Ala	Phe	Tyr	٠
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	cct	ttt	даа	atc	aaa	aac	aqc	qtq	gtg	tgt	ttg	aaa	gaa	ttt	tat	caa	576
	Pro	Phe	Glu	Ile	Lvs	Asn	Ser	Val	Val	Cys	Leu	Lys	Glu	Phe	Tyr	Gln	
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	aca	ttt	ma a		gat	tta	aac	att	tta	σασ	cct	gaa	cac	atc	qct	aag	624
	NI a	Phe	Glu	Lve	Asp.	Len	Glv	Val	Leu	Glu	Pro	Glu	Ara	Ile	Ála	Lys	
	ATG	FILE	195	Dys	, 10 P	200	,	200					205		•	-	
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	aaa	Phe	רבר	aac Aac	cor	Lou	yea Val	Glo	Tla	Tla	Thr	Mla	Len	Tle	Val	Pro	
	гÀг		Pne	Maii	Ser	neu	215	014	110	110		220	200				
		210						+~~		~~~	~~~		+++	tac	220	caa	720
	ttt	aaa	gag	cat	gtg	gra	gra	Cyc	con	999	21	y cy	Dho	Cyc	Aen	Gla	
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	Leu	Leu	Cys	Glu		Leu	ATa	глs	Arg		Arg	GIÀ	ren	гÃ2	Arg	GIII.	
					245					250		•			255	- 4	03.0
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	Tyr	Phe	Phe	His	Lys	His	Phe	Pro		Asn	Asp	Ser	Ser	Ile	Pro	TTG	
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		0> 22															
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	_	GIH	176.0	1120	5			••••		10					15		
	1	His	210	u i a	Dho	Tau	al a	Sor	V=1		Aen	Δla	I.en	T.eu	Gln	Asp	
	Hls	HIS	ATG			теп	vra	Ser	25	пец	тэр	ALG	LCu	30	·		
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	Leu	I.vs	His	Gln	Leu	Asn	Lys	Leu	Leu	Lys	Arg	Val	Gln	Lys	His	Phe	
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105
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Phe Ser Leu Asp Leu Thr Gly Thr Ile Ser Phe Glu Ala Glu Ser Gly
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Pro Phe Glu Ile Lys Asn Ser Val Val Cys Leu Lys Glu Phe Tyr Gln
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Ala Phe Glu Lys Asp Leu Gly Val Leu Glu Pro Glu Arg Ile Ala Lys
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                            200
Lys Phe Phe Asn Ser Leu Val Glu Ile Ile Thr Ala Leu Ile Val Pro
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Phe Lys Glu His Val Val Val Cys Ser Gly Gly Val Phe Cys Asn Gln
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Leu Leu Cys Glu Gln Leu Ala Lys Arg Leu Arg Gly Leu Lys Arg Gln
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Tyr Phe Phe His Lys His Phe Pro Pro Asn Asp Ser Ser Ile Pro Ile
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Cys Asp Leu Asp Tyr Ile Pro Asn Ala Ala Arg Glu Lys Arg Val Asp
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Val	cat His	ttt Phe	aaa Lys	gaa Glu	aat Asn 70	qca	gag Glu	agc Ser	gtt Val	aat Asn 75	tta Leu	caa Gln	ggg Gly	gtt Val	tct Ser 80	240
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Val 305					310					312					320	
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Lys	Asn	Cys		Leu	Gry	Буз		345	-1-				350	-		
			340											+	~~~	1104
aat	ttt	tcc	aac	act	tca	ggc	tat	aga	gct	tta	gaa	agc	cac	cat	gca	1104
200	200	60-	Acn	Thr	Ser	GIV	Tvr	Ara	Ala	Leu	Glu	Ser	His	His	Ala	
Asn	Pne	Ser	ASII	IIII	Der	0-3	360	3				365				٠
		355					300							~~~	asc.	1152
agc	ata	cat	gct	gaa	gct	aat	gat	ttg	gtt	aaa	gcc	ycc	Caa	gaa	gac	2200
Ser	va i	His	Ala	Glu	Ala	Asn	Asp	Leu	Val	Lys	Ala	val	GIn	GIU	Asp	
261						375	_				380					
	370						a+ a	~~~	cat	222	ata	cat	tta	atq	gaa	1200
cac	att	acc	gat	tca	aaa	Lac	- CLA	909	114.0	T	V-1	Hie	T.Au	Mot	Ğlu	
His	Ile	Thr	Asp	Ser	Lys	Tyr	Leu	GIU	HIS	гÀг	Val	ura	Dea	Mec	Glu 400	
205					390					222						
		aat	222	cat	att	aga	даа	aat	att	qat	aag	atg	ttt	tac	gaa	1248
gat	agt	gec	-	772 -	17-1	722	Clu	λen	Tle	Asp	Lvs	Met	Phe	Tyr	Glu	
Asp	Ser	Ala	Lys		vaı	Arg	GIU	Maii	110	TOP	-,,			415		
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	C22	gat	gaa	ctc	aat	aaa	atc	att	gaa	aaa	att	caa	aaa	ggc		1293
aaa	Caa	3	61.	Lou	Aen	LVS	Tle	Tle	Ğlu	Lvs	Ile	Gln	Lys	Gly		
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_		Mon	цуз	Ü	200				10					15)	
1				. 5	_		** - 7			~	Gln	Ser	T.eu	Len	Asn	
Ile	Ala	Glu	Leu	Lys	ьys	GIU	vaı	ASII	Dea	ıyı	GIII	002	200		Asn	
			20					25					30	,		
Tou	Cue	T.e.11	His	Glu	Glv	Phe	Val	Gly	Ile	Lys	Asn	Asn	Lys	var	Val	
neu	Cys				3		40	_				45				
		35		_	•			T 011	n en	Aen	T.em	Glu	Glu	Gln	Ser	
Phe	Lys	Ser	. CTA	Asn	Leu	ALG	ser	Den	Poli	71311					Ser	
	EΛ					55					90					
V-1	Hic	Phe	Lvs	Glu	Asn	Ala	Glu	Ser	Val	Asn	Leu	Gin	GT?	, vai	Ser 80	
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65	1	_	_		01-		Tla	Non.	Gly	۷al	Gln	Tvr	Phe	Ser	Leu	
Tyr	Ser	Lev	ı Lys	Ser	GIL	ASI	116	wah	GIY	• • • •	· • • • • • • • • • • • • • • • • • • •	-3-		95	Leu	
				85					90					,	•	
710	1.00	AST	Thr	Ser	Cvs	Val	Gly	Glu	Tyr	His	Lys	AST	Asp	Let	ı Phe	
			100					11115						,		
			100		_			C1.	C1.	Ten	Gli	Asn	Ala	Glr	ı Glu	
Lys	Thr	: Phe	: Cys	ALA	Ser	Lec	гъ	GIU	GIY	пси	. 020	125				
		115					120	,				1				
	- Mat	- Glr	TVI	Phe	His	Glr	Glu	Thr	Gly	Ala	Lev	ı Leu	ASI	J ATS	a Ala	
261						135					140)				
	130	,				0	, mb		C111	T.e.	GIV	Thr	· Va	l Asr	160	
Lys	: Asr	ı Gly	/ Glu	i ATa	HIS	s Ser	Int	GIU	GLY	Dec	. 01				160	
					15/	`				133	,					
mb.	. Glv	, G1:	Ast	Tle	Glu	Ser	Lev	Tyr	Glu	Lys	: Met	: Glr	ASI	u Ale	a Thr	
1111	GI	, 01.		165				-	170					175	5	
				105	' _		1			Acr	Gly	11e	Th	r Gli	n Val	·.
Se	c Let	ı Ala	a Asp	, Ser	: Let	AST	i GI	Arg	Ser	- ASI	. 010		19	n	n Val	
			180	1				193)					•		
-1		- T.O.	. 114	Agr	Ast	116	Ala	Glu	. Gln	Thr	: Asr	ı Let	ı Le	n AT	a Leu	
TTG	3 Se.			·	,		200	\ \				205	, ·			
		19	5				200	, 			. 114.			a G1:	y Phe	
Agr	a Ala	a Ala	a Ile	e Glu	ı Ala	a Ala	Arc	J ATS	r et	GIL	, nr	, Gr	' UT,	9	y Phe	
	01/	^				יוכ	•				221	,				
		1 11-	יות ו	. 7	, G1.	, Val	Arc	T.V	Leu	Ala	Glu	ı Lys	Th:	r Gl	n Lys	
Al:	a va.	r va	r WT	a wal	911	. va.		, ~, -		235	,	•			240	
22	5				230	J				435	, - \.	. 61-		n (1)		
ומ	a Th	r Lv	s Gl	ı Ile	ala e	a Va.	l Val	L Val	Lys	Sei	. Met	. GII	i GT	i GT	u Ala 5	
				245	5				254	,					_	
_	_	_ +1	~ C1-	. mb-	r Nov	ማኮነ	- Hic	Agr	Ile	Asr	Sei	r Ile	e Va	l Se	r Ser	
As	n As	b 11	e GII	ı ını	. ASI	1 111		, 110}								

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265
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Ile Lys Gly Asp Val Glu Glu Leu Lys Ser Thr Val Lys Asn Asn Met
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Val Phe Cys Gly Leu Ala Lys Leu Asp His Val Val Phe Lys Asn Asn
                                        315
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Leu Tyr Gly Met Val Phe Gly Leu Asn Ser Phe Asp Ile Thr Ser His
                                    330
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Lys Asn Cys Arg Leu Gly Lys Trp Tyr Tyr Glu Gly Ala Gly Lys Glu
                                345
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Asn Phe Ser Asn Thr Ser Gly Tyr Arg Ala Leu Glu Ser His His Ala
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Ser Val His Ala Glu Ala Asn Asp Leu Val Lys Ala Val Gln Glu Asp
                                             380
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His Ile Thr Asp Ser Lys Tyr Leu Glu His Lys Val His Leu Met Glu
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gaa tac gct tac aag gtt tat ggc gca gtg gtg agt caa aat aaa gac
Glu Tyr Ala Tyr Lys Val Tyr Gly Ala Val Val Ser Gln Asn Lys Asp
                                 25
ggc gtg tgg gtc ggc gat gaa gcc aaa acg aaa gcc aga aga aaa gaa
Gly Val Trp Val Gly Asp Glu Ala Lys Thr Lys Ala Arg Arg Lys Glu
                              40
         35
att ctt gaa aac aga aag gct aga tcc ata ccg gta aaa caa tgg atg
                                                                   192
Ile Leu Glu Asn Arg Lys Ala Arg Ser Ile Pro Val Lys Gln Trp Met
                                              60
                         55
                                                                   240
gag caa gaa aga aac gct atc ctt gaa aaa gag gct tcc aaa cag gtt
Glu Gln Glu Arg Asn Ala Ile Leu Glu Lys Glu Ala Ser Lys Gln Val
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 Ile Leu Glu Asn. Arg Lys Ala Arg Ser Ile Pro Val Lys Gln Trp Met
                                              60
                          55
 Glu Gln Glu Arg Asn Ala Ile Leu Glu Lys Glu Ala Ser Lys Gln Val
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80
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Lys His Met Tyr Ala Thr Ser Phe Asp Leu Ser Pro Lys Phe Leu
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Arg Arg Asn Gln Lys Ser Ala Ser Lys Phe Ile Asn Tyr Pro Ser Lys
                                     10
tto tto act cta tgc tat aat ctc tgt ttt aaa aca tta tgg aat gtt
                                                                    96
Phe Phe Thr Leu Cys Tyr Asn Leu Cys Phe Lys Thr Leu Trp Asn Val
             20
aga aga tat toa goa aaa coo tto caa aco aac caa tot aaa gaa aga
Arg Arg Tyr Ser Ala Lys Pro Phe Gln Thr Asn Gln Ser Lys Glu Arg
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Phe Phe Thr Leu Cys Tyr Asn Leu Cys Phe Lys Thr Leu Trp Asn Val
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Arg Arg Tyr Ser Ala Lys Pro Phe Gln Thr Asn Gln Ser Lys Glu Arg
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 aaa gaa agc gtt cag cct aaa aat ggc gtt tta gcg gaa gtg gta gaa
                                                                    96
Lys Glu Ser Val Gln Pro Lys Asn Gly Val Leu Ala Glu Val Val Glu
                                 25
             20
 tct agc gat tta gtg caa agc gcg att gat ttg att gtt aaa agt tcg
                                                                    144
 Ser Ser Asp Leu Val Gln Ser Ala Ile Asp Leu Ile Val Lys Ser Ser
                                                  45
                              40
         35.
 gtt aaa aaa ctc ttt ttt gac ccc aat caa gtg aat tta caa acc tac
                                                                    192
 Val Lys Lys Leu Phe Phe Asp Pro Asn Gln Val Asn Leu Gln Thr Tyr
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                                                                    222
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Leu Gly Tyr Asn Met Ala Leu Met Ala Met Val Asn Ile Leu Ala Glu
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                  5
 1
atg aaa gcg ttc caa gaa gcc caa aaa aac aac cct aat aac ccc att
                                                                    96
Met Lys Ala Phe Gln Glu Ala Gln Lys Asn Asn Pro Asn Asn Pro Ile
             20
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aac aat caa aaa
Asn Asn Gln Lys
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Asn Asn Gln Lys
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Ser Lys Glu Ser Leu Met His Ala Ile Asn Ser Ile Arg Val Gly Met
                                      10
 cat ttt aaa gag ttg agt cag att tta gag agc act att aca gaa agg
His Phe Lys Glu Leu Ser Gln Ile Leu Glu Ser Thr Ile Thr Glu Arg
                                  25
             20
 ggc ttt gtg cct ttg aaa gga ttt tgc ggg cat ggc att ggt aaa aaa
 Gly Phe Val Pro Leu Lys Gly Phe Cys Gly His Gly Ile Gly Lys Lys
 ccc cat gaa gag cca gag atc ccc aac tac cta gaa aaa ggc gtc aaa
                                                                    192
 Pro His Glu Glu Pro Glu Ile Pro Asn Tyr Leu Glu Lys Gly Val Lys
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			•													
Pro	aat Asn	agc Ser	ggc Gly	cct Pro	Lys	atc Ile	aaa Lys	gag Glu	ggc Gly	atg Met 75	gta Val	ttt Phe	tgc Cys	tta Leu	gag Glu 80	240
65 cct Pro	atg Met	gtg Val	tgt Cys	caa Gln	70 aaa Lys	cag Gln	ggc Gly	gag Glu	cct Pro	aaa	ata Ile	cta Leu	gcg Ala	Asp	aag	288
taa	200	gtg Val	att	85 tca	ata	gat	aga	ctt	90 aac	aca	agc	cac	cat	gag	cat	336
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		Val 35					40					45				
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		Val		85					90					95		
_		Val	100					105					110		HIS	
Thr	Ile	Ala 115	Ile	Val	Gly	Asn	Lys 120	Ala	Val	Ile	Leu	125	GIU	Arg		
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1				5					10					13		96
gcg Ala	aat Asn	tgc Cys	Pro	Asp	Leu	Leu	Leu	Cys	Asp	Glu	Ala	Thr	Ser 30	Ala	Leu	,,,
gat	tct	aaa	20 acc	acq	cat	tct	att	tta	acg	ctt	tta	agc	ggc	att	caa	144
_		35					40					45			Gln	102
aaa Lys	aag	ctt Leu	gat Asp	ttg Leu	agc Ser	atc Ile	gtt Val	ttc Phe	atc Ile	acg Thr	Cat His	gaa Glu	Ile	Glu	Val	.192
-	50					55					60				atc	240
Val	Lys	Glu	Leu	Cys	Asn 70	Gln	Met	Cys	Val	Ile 75	Ser	Ser	ĞÎy	Ğlu	Ile 80	
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1 y 1	GLY	Буз	02	5					10					15		
	++~	aat	caa	acc	ctt	σat	aaa	ata	aac	tct	agc	tct	gat	gcc	aaa	96
gge	Tan	non	Gla	Ala	Len	Asp	Lvs	Ile	ĞÎv	Ser	Ser	Ser	Asp	Ala	Lys	
GIĀ	Leu	ASII	20	,,,,,			-,-	25					30			*
			20	++~	tta	nat	222		act	ttt	aaa	gat	att	tta	aat	144
gac	tta	Cay	aac aac	Dho	Tan	Den.	Luc	Thr	Thr	Phe	Ğĺv	Asp	Ile	Leu	Asn	
Asp	Leu		ASII	FIIE	Dea	Asp	40		• • • •		3	45				
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caa	atg	att	gaa	Caa	312	Dro	Ton	Tla	Acn	Lvs	Leu	Ile	Ser	Trp	Leu	
Gln			GIU	GIII	MIG	55	Dea	110	,,,,,,	2,0	60					
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ggt	ccg	cag	gat	ttg	age	ycc val	LLa	yry Val	Aen	Tle	Ala	Leu	Asn	Ser	Ile	
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65		141			70						tot	200	ata	aat	-	288
act	aac	cct	agt	aaa	gag	ctg	mb-	age	Thr	Tla	Sor	Ser	Tle	ggt Gl v	Glu	•
Thr	Asn	Pro	Ser		GIU	ren	Int	Ser	90	116	Jer	501		Gly 95		
				85						-+-	a+ a	2 2 t	222		ato	336
aaa	gcg	tta	aat	gac	tta	tta	ggc	gat	ggc	gua	ycy 17-1	A a n	Luc	atc	Met	550
Lys	Ala	Leu		Asp	Leu	Leu	GIA	Asp	GIÅ	· vai	Val	non	110	Ile	1100	
			100					105							226	384
agc	aat	caa	gtc	tta	ggg	caa	atg	atc	aat	aaa	atc	all Tla	31.	gat	Tue	304
Ser	Asn	Gln	Val	Leu	Gly	Gln	Met	IIe	Asn	гÀг	TIE	176	WIG	Asp	Lys	
		115					120					125				432
ggc	ttt	gga	ggc	gtt	tat	cag	caa	ggt	tta	ggc	tcc	ata	CLY	cct	Cla	432
Gly	Phe	Gly	Gly	Val	Tyr	Gln	Gln	Gly	Leu	GIA	Ser	TIE	Leu	Pro	GIII	
_	130					135					140					477
tct	tta	caa	gat	gaa	ttg	aag	aaa	ttg	ggc	atg	ggc	tct				471
Ser	Leu	Gln	Asp	Glu	Leu	Lys	Lys	Leu	Gly	Met	Gly	Ser				•
145					150					155						•
	0> 2	42														
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	2> P															
761 791	3> n	elic	obac	ter	olva	ri										
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< 4 U	0> 2	, 7	(C) ~	Ser	וום.]	Ser	Ser	Phe	Ala	Asn	Asn	Phe	Val	Pro	Gly	
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1			O1	- ות	T	Z or	Luc	Tle			Ser	Ser	Asp	Ala	Lvs	
Gly	Leu	Asn			neu	nap	n y S	25	y	JUL			30			
			20	n:	Υ	7	7			Pho	610	Den			Asn	
Asp	Leu			rne	reu	Asp	PAS	1111	THE	T. 11G	0 ± y	45			Asn	
		35				_	40		N	T	T 011			Trn	Ĩ,en	
Gln	Met	: Ile	Glu	Gln	Ala	Pro	Leu	тте	ASD	пA2	rea	TTG	261	rrp	Leu	

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Gly Pro Gln Asp Leu Ser Val Leu Val Asn Ile Ala Leu Asn Ser Ile
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Thr Asn Pro Ser Lys Glu Leu Thr Ser Thr Ile Ser Ser Ile Gly Glu
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Lys Ala Leu Asn Asp Leu Leu Gly Asp Gly Val Val Asn Lys Ile Met
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Ser Asn Gln Val Leu Gly Gln Met Ile Asn Lys Ile Ile Ala Asp Lys
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Gly Tyr Ala Leu Ala Gly Ser Ser Ala Asn Phe Glu Phe Lys Ala Gly
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Thr Asp Thr Lys Asn Gly Thr Ala Thr Phe Asn Asn Asp Ile Ser Leu
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                              40
gga aga ttt gtg aat tta aaa gtg gat gct cat aca gct aat ttt aaa
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Gly Arg Phe Val Asn Leu Lys Val Asp Ala His Thr Ala Asn Phe Lys
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ggt att gat act ggt aat ggt ggt ttc aac acc tta gat ttt agt ggc
Gly Ile Asp Thr Gly Asn Gly Gly Phe Asn Thr Leu Asp Phe Ser Gly
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 Thr Asp Thr Lys Asn Gly Thr Ala Thr Phe Asn Asn Asp Ile Ser Leu
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acc	aat Asn	ggg	agc	aat	aaa	acg	Sor	999 C1v	Aen	Asn	Cvs	Tvr	Glu	Pro	Asn	
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Pro	val	275		GIII	TÄT	ALG	280		_,_			285		•		
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ago	Asn	Glv	Leu	Glv	Val	ĞÎv	Leu	ĞÎy	Tyr	Lys	Tyr					
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Gln Lys Val Tyr Asn Asp Ala Gln Lys Ile Ala Asn Ile Ile Ala Ser
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Asn Leu Leu Thr Glu Phe Ile Lys Thr Ala Gly Phe Ile Gln Asn Asn
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Asp Ser Ser Val Ser Thr Ser Leu Thr Ser Ala Phe Gln Ala Ile Thr
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Ile Gln Ser Phe Ser Gln Thr Leu Arg Gln Leu Leu Gly Asp Lys Thr
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Arg	Lys	Arg	Tyr	Glu	Asp	Phe	Leu 40	Lys	Asn	Asp	Tyr	45	гÀ2	TTE	ren	
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	5.0	Asr	n Asr			55	<u> </u>				60	,			Ile	
6	Let	ılle			70)				/3)				Ser 80	
Phe	. G1			S S	5				90)				95		
			100	Ile	Ile			105)				11/	,	Gln	
		111	c Ile	e Asr			120)				123	•		Glu	
Ile	Ty:	Asp	Ty:	r Arg	g Ile	e Gly	/ Gly	, Tyr	Gly	Val	. Leu	ı Asp	Lys	Туг	Leu	

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Ile	-			165					170					113		
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vaı	Asp	гÀг	420	neu	Glu	nis										
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               165
Gln Gly Val Lys His Leu Thr Asn Glu Glu Ala Ala Glu Val Arg Lys
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                                185
Tyr Asp Pro Asp Ser Asn Gln Arg Asp Leu Phe Asn Ala Ile Ala Arg
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Gly Asp Phe Pro Lys Trp Lys Leu Ser Ile Gln Val Met Pro Glu Glu
                        215
    210
Asp Ala Lys Lys Tyr Arg Phe His Pro Phe Asp Val Thr Lys Ile Trp
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                    230
Tyr Leu Gln Asp Tyr Pro Leu Met Glu Val Gly Ile Val Glu Leu Asn
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Lys Asn Pro Glu Asn Tyr Phe Ala Glu Val Glu Gln Ala Ala Phe Ser
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Pro Ala Asn Val Val Pro Gly Ile Gly Tyr Ser Pro Asp Arg Met Leu
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Gln Gly Arg Leu Phe Ser Tyr Gly Asp Thr His Arg Tyr Arg Leu Gly
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Val Asn Tyr Pro Gln Ile Pro Val Asn Lys Pro Arg Cys Pro Phe His
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Ser Ser Ser Arg Asp Gly Tyr Met Gln Asn Gly Tyr Tyr Gly Ser Leu
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                                     330
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Gln Asn Tyr Thr Pro Ser Ser Leu Pro Gly Tyr Lys Glu Asp Lys Ser
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Ala Arg Asp Pro Lys Phe Asn Leu Ala His Ile Glu Lys Glu Phe Glu
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Val Trp Asn Trp Asp Tyr Arg Ala Asp Asp Ser Asp Tyr Tyr Thr Gln
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Pro Gly Asp Tyr Tyr Arg Ser Leu Pro Ala Asp Glu Lys Glu Arg Leu
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 Arg Ile Ala Asp Leu Met Gln Lys Asp Ala Asn Glu Val Tyr Arg Leu
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 aaa aag ctt tcc act ttt caa gag ctt gtg agc gtg tat tac ggc atg
 Lys Lys Leu Ser Thr Phe Gln Glu Leu Val Ser Val Tyr Tyr Gly Met
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 gtg tta aac gca gaa gtg gct gaa act tta gaa gag gtg gaa aaa ggc
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 Val Leu Asn Ala Glu Val Ala Glu Thr Leu Glu Glu Val Glu Lys Gly
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 His Tyr Lys His Phe Gln Asn Ala Leu Lys Met Gln Lys Val Gly Gln
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 atc gct agg gta gaa acc tta ggc gct caa gtg gct tat gat aag gcc
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 Ile Ala Arg Val Glu Thr Leu Gly Ala Gln Val Ala Tyr Asp Lys Ala
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Ser	Phe	Asn 115	Ser	Ile	Leu	Ser	Ser 120	Lys	Asp	Asp	Leu	Val 125	Pro	Ser	Ser	
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Sér	Val	Phe 195	Glu	Asp	Met	Ile	Pro 200	Ser	Trp	Phe	Val	Gly 205	Val	Ala	Gly	•
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Arg	Met 210	Pro	Ile	Leu	Ser	Pro 215	Thr	Gly	Arg	Ile	Gln 220	Lys	Tyr	Gln	Ala	
agc	aaa	tta	gcg	gag	ttg	caa	gtg	agt	agc	gaa	caa	atc	cag	gct	aaa	720
Ser 225	Lys	Leu	Ala	Glu	Leu 230	Gln	Val	Ser	Ser	Glu 235	Gln	Ile	Gln	Ala	Lys 240	·
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Tyr	Leu	Lys	Glu 260	Tyr	Lys	Ser	Leu	Leu 265	Ser	Ser •	Val	Glu	Leu 270	Ala	Lys	
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gag	caa	aaa	agc	gtg	gct	tat	aaa	tac	atc	gtt	tca	tta	gcg	aat	tta	960
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_	-	Leu 35					40					45				
	50					55	•				60					
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His Ile Ala Ser Val Lys Ala Lys Asp Val Leu Glu Val Ser Gln Leu
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Lys Leu Glu Ile Arg Thr Glu Lys Asn Leu Pro Asp Leu Ser Phe Phe
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Val Ser Ser Thr Leu Asn Ser Tyr Pro Val Leu Lys Thr Leu Glu Asn
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                    150
Gln Ile Gln Ile Ser Lys Glu Asn Thr Lys Leu Gln Ile Ala Lys Phe
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Leu Pro Gln Val Ser Phe Phe Gly Ser Tyr Ile Met Lys Gln Asn Asn
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Ser Val Phe Glu Asp Met Ile Pro Ser Trp Phe Val Gly Val Ala Gly
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Arg Met Pro Ile Leu Ser Pro Thr Gly Arg Ile Gln Lys Tyr Gln Ala
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                        215
Ser Lys Leu Ala Glu Leu Gln Val Ser Ser Glu Gln Ile Gln Ala Lys
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Lys Asn Met Glu Leu Leu Val Asn Lys Thr Tyr Lys Glu Thr Leu Ser
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Tyr Leu Lys Glu Tyr Lys Ser Leu Leu Ser Ser Val Glu Leu Ala Lys
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                                265
Glu Asn Leu Lys Leu Gln Glu Gln Ala Phe Leu Gln Gly Leu Ser Thr
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Asn Ala Gln Val Ile Asp Ala Arg Asn Thr Leu Ser Ser Ile Val Val
                        295
Glu Gln Lys Ser Val Ala Tyr Lys Tyr Ile Val Ser Leu Ala Asn Leu
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gcc gct att gaa gcc gca agg gcc ggc gag cat ggc aga ggc ttt gcg
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Ala Ala Ile Glu Ala Ala Arg Ala Gly Glu His Gly Arg Gly Phe Ala
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gtg gtg gct gat gag gta aga aag ctc gct gaa agg acg caa aaa tcg
                                                                   144
Val Val Ala Asp Glu Val Arg Lys Leu Ala Glu Arg Thr Gln Lys Ser
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ctc agc gag att gaa gcc aat atc aat att tta gtg caa agc att tca
Leu Ser Glu Ile Glu Ala Asn Ile Asn Ile Leu Val Gln Ser Ile Ser
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gac acg agc gaa agc att aaa aac cag gtt aaa gaa gtg gaa gaa atc
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Asp Thr Ser Glu Ser Ile Lys Asn Gln Val Lys Glu Val Glu Glu Ile
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                                         75
aac gct tct att gaa gcc tta aga tcg gtt act gag ggc aat cta aaa
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Asn Ala Ser Ile Glu Ala Leu Arg Ser Val Thr Glu Gly Asn Leu Lys
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atc gct ag
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Leu Ser Glu Ile Glu Ala Asn Ile Asn Ile Leu Val Gln Ser Ile Ser
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Asp Thr Ser Glu Ser Ile Lys Asn Gln Val Lys Glu Val Glu Glu Ile
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Leu Ser Ser Val Leu Glu Thr Val Arg Ile Ser Gln Asp Glu Ile Tyr
             20
acc gtt gat ggc aag agc gtg ttg cgt ttg aga gat gag gtg ctt tct
Thr Val Asp Gly Lys Ser Val Leu Arg Leu Arg Asp Glu Val Leu Ser
                             40
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Leu Val Arg Leu Ser Asp Ile Phe Lys Val Asp Ala Ile Leu Glu Ser
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aac tca gat gtg tat gtg gtt atc att ggc ttg gct gat caa aaa att
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Asn Ser Asp Val Tyr Val Val Ile Ile Gly Leu Ala Asp Gln Lys Ile
                                          75
gge gtg ate gtg gat tat tta ate ggt caa gaa gaa gtg gte att aaa
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Gly Val Ile Val Asp Tyr Leu Ile Gly Gln Glu Glu Val Val Ile Lys
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                                     90
tot the ggt tac tat out and and act aga ggc att get ggt gct acg
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Ser Leu Gly Tyr Tyr Leu Lys Asn Thr Arg Gly Ile Ala Gly Ala Thr
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                                105
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gtg aga ggc gat ggg aaa atc acc ctt att gta gat gtg ggg gcg atg.
Val Arg Gly Asp Gly Lys Ile Thr Leu Ile Val Asp Val Gly Ala Met
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                                                 125
        115
atg gat atg gca aaa agc atc aag gtc aat atc act acc tta atg a
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Gly Val Ile Val Asp Tyr Leu Ile Gly Gln Glu Glu Val Val Ile Lys
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                 85
Ser Leu Gly Tyr Tyr Leu Lys Asn Thr Arg Gly Ile Ala Gly Ala Thr
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Glu Ala Leu Thr Arg His Met Ser Lys Asp Tyr Asp Met Ala Val Ile
                                  25
act aat gat att tac acg aaa gaa gac gca gag ttt atg tgt aaa aat
Thr Asn Asp Ile Tyr Thr Lys Glu Asp Ala Glu Phe Met Cys Lys Asn
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                                                                    240
 Pro His Thr Ala Ile Arg Glu Asp Ala Ser Met Asn Leu Glu Ala Val
                                          75
 gaa gaa atg cat ggc cgt ttc cct aat ttg gaa ttg ctt ttg att gaa
                                                                    288
 Glu Glu Met His Gly Arg Phe Pro Asn Leu Glu Leu Leu Ile Glu
                                      90
                 85
 age gga gge gat aac ett tea geg aca tte aac eea gag eta geg gae
                                                                    336
 Ser Gly Gly Asp Asn Leu Ser Ala Thr Phe Asn Pro Glu Leu Ala Asp
                                 105
             100
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 Phe Thr Ile Phe Val Ile Asp Val Ala Glu Gly Asp Lys Ile Pro Arg
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 Lys Gly Gly Pro Gly Ile Thr Arg Ser Asp Leu Leu Val Ile Asn Lys
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 Asp Ser Lys Lys Met
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		35		Val			40					43				
	50	Ser		Ala		55					90	-				
66	His			Leu	70					15					80	
Pro				Pro 85			_		90					93		
			100	Ser				105					110			
Ser	Met	Pro 115	His	Ser	Glu	Pro	Asn 120	Phe	Lys	Val	Ser	Leu 125	Ala	Ser	Asp	
Phe	Lys 130		Val	Val	Lys											
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	1> 6		,						•							
	2> Di															
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Ile	Lys	Arg	Ala	Ala	Lys	Glu	Leu	Lys	Glu 10	Gly	Met	Tyr	Val	Asn 15		
1				CCC	200	ctt	ata	act		σaa	ata	agc	ggg		_	96
ggg	ata	ggc	T.e.11	Pro	Thr	Leu	Val	Ala	Asn	Ğlu	val	Ser	Gly	Met	Asn	
_			20					25					30			
ato	att	ttc	caa	age	gag	aac	ggg	ctg	tta	ggg	att	ggc	gct	tac	cct	144
Ile	Val	Phe	Gln	Ser	Glu	Asn	GLY 40	Leu	Leu	GIY	TTE	45	ATO	171	110	3.00
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Lev	Glu	Gly	Ser	Val	Asp	Ala 55	Asp	Leu	TTE	Asn	60	GIĀ	пåэ	GIU		
ata		~+~	gtg	ccg	ggc	gct	tcg	ttt	ttc	aat	agc	gcg	gat	tcg	ttt	240
Ile	Thr	Val	Val	Pro	Gly	Ala	Ser	Phe	Phe	Asn	Ser	Ala	Asp	Ser	Phe 80	
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gcg	atg	att	cgt	ggg	ggg	cat	att	gat	LLa	Ala	Ile	Leu	Glv	Gly	atg Met	
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gaa	gto	tca	caa	aat	ggg	gat	ttg	gct	aat	tgg	atg	atc	CCT	aaa	aag	330
Glu	val	Ser	Gln	Asn	Gly	Asp	Leu	Ala 105	Asn	Trp	met	116	110	пуз	Lys	
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CTO	, Tle	Lus	: Glu	Met	Glv	Glv	Ala	Met	Asp	Leu	Val	His	Gly	Ala	Lys	•
		115			•		120	l				12.				432
aaa	gtg	att	gtg	atc	atg	gag	cat	tgc	aac	aaa	tac	ggg	gag	COL	aaa	432
Ly	val	. Ile	· Val	Ile	Met	GLu	His	Cys	Asn	Lys	140	GTA	GIU	Ser	Lys	
	130)				135		. ++=	202	aaa			ato	ato	cat	480
gt	g aaa	aag	gaa	tgo	CO	· Tan	Dro	Len	Thr	Glv	Lvs	Glv	Val	Val	cat His	
4.41	=				150)				122)				100	
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Ca:	a LUŞ n J.el	, ace	Thr	Asp	Lev	Ala	Val	Phe	Glu	Phe	Ser	Asr	Asn	Wie	HICC	
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Ly	s Lev	ı Val	l Glu	ı Lev	,Glr	Glu	Gly	, var	Ser	Leu	ASP	GIL	190	. Dys	Glu	
			180)				185	٠.				130	•	•	

606 aag aca gaa gct gaa ttt gag gtg cgc tta Lys Thr Glu Ala Glu Phe Glu Val Arg Leu 195 <210> 266 <211> 202 <212> PRT <213> Helicobacter pylori <400> 266 Ile Lys Arg Ala Ala Lys Glu Leu Lys Glu Gly Met Tyr Val Asn Leu Gly Ile Gly Leu Pro Thr Leu Val Ala Asn Glu Val Ser Gly Met Asn 25 Ile Val Phe Gln Ser Glu Asn Gly Leu Leu Gly Ile Gly Ala Tyr Pro 40 Leu Glu Gly Ser Val Asp Ala Asp Leu Ile Asn Ala Gly Lys Glu Thr 55 Ile Thr Val Val Pro Gly Ala Ser Phe Phe Asn Ser Ala Asp Ser Phe 75 70 Ala Met Ile Arg Gly Gly His Ile Asp Leu Ala Ile Leu Gly Gly Met 90 85 Glu Val Ser Gln Asn Gly Asp Leu Ala Asn Trp Met Ile Pro Lys Lys 105 100 Leu Ile Lys Gly Met Gly Gly Ala Met Asp Leu Val His Gly Ala Lys 120 115 Lys Val Ile Val Ile Met Glu His Cys Asn Lys Tyr Gly Glu Ser Lys 140 135 Val Lys Lys Glu Cys Ser Leu Pro Leu Thr Gly Lys Gly Val Val His 155 150 Gln Leu Ile Thr Asp Leu Ala Val Phe Glu Phe Ser Asn Asn Ala Met 170 165 Lys Leu Val Glu Leu Gln Glu Gly Val Ser Leu Asp Gln Val Lys Glu 185 180 Lys Thr Glu Ala Glu Phe Glu Val Arg Leu 195 <210> 267 <211> 336 <212> DNA <213> Helicobacter pylori <220> <221> CDS <222> (1)..(336) <400> 267 ggg att gaa caa gac gct gat att gtt tta ttt tta tat aga ggc tat 48 Gly Ile Glu Gln Asp Ala Asp Ile Val Leu Phe Leu Tyr Arg Gly Tyr atc tat caa atg agg gct gaa gac aac aaa ata gac aaa ctc aaa aaa 96 Ile Tyr Gln Met Arg Ala Glu Asp Asn Lys Ile Asp Lys Leu Lys Lys 25 20 gaa ggt aaa att gaa gag gcg caa gag ttg tac tta aaa gtt aat gaa Glu Gly Lys Ile Glu Glu Ala Gln Glu Leu Tyr Leu Lys Val Asn Glu 35 gaa agg cgt atc cac aag caa aat ggc agc att gaa gag gct gaa atc Glu Arg Arg Ile His Lys Gln Asn Gly Ser Ile Glu Glu Ala Glu Ile 55 50 att gtg gct aaa aac agg aat ggg gct aca gga acg gtt tat acg cgc 240 Ile Val Ala Lys Asn Arg Asn Gly Ala Thr Gly Thr Val Tyr Thr Arg 65 ttt aac get eet tte acg ege tat gaa gae atg eee ata gat tee cat 288 Phe Asn Ala Pro Phe Thr Arg Tyr Glu Asp Met Pro Ile Asp Ser His 90 85 tta gaa gaa ggg caa gaa act aaa gtg gat tat gat ata gtt aca act

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Glu Gly Lys Ile Glu Glu Ala Gln Glu Leu Tyr Leu Lys Val Asn Glu
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Glu Arg Arg Ile His Lys Gln Asn Gly Ser Ile Glu Glu Ala Glu Ile
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Ile Val Ala Lys Asn Arg Asn Gly Ala Thr Gly Thr Val Tyr Thr Arg
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Leu Leu Glu His Val Gln Lys Ala Leu Asn Gln Met Ser Glu Arg Glu
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caa atc ctt atc cag ctt tat tac ttt gaa gag ttg aat ttg agc gag
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Gln Ile Leu Ile Gln Leu Tyr Tyr Phe Glu Glu Leu Asn Leu Ser Glu
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Ile Lys Glu Ile Leu Gly Ile Thr Glu Ser Arg Ile Ser Gln Ile Ile
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                                                                   96
Asn Gly Val Phe Glu Ser Ser Gly Gly Arg Val Ile Phe Ala Ile Gly
                                 25
agg gga aaa too tta tta gaa goo aga aac cat got tat gaa atc got
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Arg Gly Lys Ser Leu Leu Glu Ala Arg Asn His Ala Tyr Glu Ile Ala
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Gln Lys Val His Phe Glu Gly Met Phe Tyr Arg Lys Asp Ile Gly Phe
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atg agg ggc gat gcg caa gat gtg caa tta aac atc ggt cca aat tgc
                                                                    96
Met Arg Gly Asp Ala Gln Asp Val Gln Leu Asn Ile Gly Pro Asn Cys
                                 25
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aag tta agg atc act tcg caa tcc ttt gaa aaa atc cat aac act gaa
Lys Leu Arg Ile Thr Ser Gln Ser Phe Glu Lys Ile His Asn Thr Glu
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Asp Gly Phe Ala Ser Arg Asp Met His Ile Val Val Gly Glu Asn Ala
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Phe Lys Gly Asn Thr Thr Ile Ser Leu Arg Ser Ser Ser Gln Leu Leu
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Lys Phe Asn Arg Leu His Thr Lys Ile Ser Ile Leu Gln Asp Glu Lys
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Glu Ser Glu Gly Val Asp Gly Ala Val Ser Glu Thr Ala Ser Ser His
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                                185
            180
tta tgc gtg aaa gct tta gcg aaa ggc tca gaa ccc tta ttg cat tta
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Leu Cys Val Lys Ala Leu Ala Lys Gly Ser Glu Pro Leu Leu His Leu
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                            200
      . 195
aga gaa aaa atc gct cgc ttg gtt acg caa acc acc acg caa aag gtt
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Asp Gly Phe Ala Ser Arg Asp Met His Ile Val Val Gly Glu Asn Ala
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Phe Leu Asp Phe Ala Pro Phe Pro Leu Ile Pro Phe Glu Asn Ala His
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Phe Lys Gly Asn Thr Thr Ile Ser Leu Arg Ser Ser Ser Gln Leu Leu
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Tyr Ser Glu Ile Ile Val Ala Gly Arg Val Ala Arg Asn Glu Leu Phe
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Lys Phe Asn Arg Leu His Thr Lys Ile Ser Ile Leu Gln Asp Glu Lys
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Thr His Ile Ile Val Arg Asp Leu Gln Gly Asn Glu Arg Val Leu Ser
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Asn Glu Glu Ile Gln Lys Leu Ile Lys Glu Glu Glu Ala Lys Ile Asp
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Gly Ser Gly Phe Gly Leu Gly Ser Ala Ile Leu Gly Ser Ala Ala Gly
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gcg att tta ggg agt tat att ggt aat aag ctt ttc aat aac cct aat
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Ala Ile Leu Gly Ser Tyr Ile Gly Asn Lys Leu Phe Asn Asn Pro Asn
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tac cag caa aac gcc caa cgg acc tac aaa tcc cca caa gct tac caa
                                                                   336
Tyr Gln Gln Asn Ala Gln Arg Thr Tyr Lys Ser Pro Gln Ala Tyr Gln
                                105
                                                    110
cgc tct caa aat tcc ttt tct aaa agt gcg ccc agt gct tca agc atg
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Arg Ser Gln Asn Ser Phe Ser Lys Ser Ala Pro Ser Ala Ser Ser Met
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Gly Ser Gly Phe Gly Leu Gly Ser Ala Ile Leu Gly Ser Ala Ala Gly
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Ala Ile Leu Gly Ser Tyr Ile Gly Asn Lys Leu Phe Asn Asn Pro Asn
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Tyr Gln Gln Asn Ala Gln Arg Thr Tyr Lys Ser Pro Gln Ala Tyr Gln
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gat caa gcc ccc ata ggc aaa acc cca cga agc aac cct gcc act tac
Asp Gln Ala Pro Ile Gly Lys Thr Pro Arg Ser Asn Pro Ala Thr Tyr
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Ala Lys Ile Leu Gly Tyr Ser Ala Ser Arg Phe Ser Phe Asn Val Lys
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Met His Phe Leu Pro Asp Val Leu Val Gln Cys Asp Ser Cys Lys Gly
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                                                                   384
Ala Lys Tyr Asn Pro Gln Thr Leu Glu Ile Lys Val Lys Gly Lys Ser
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Ala Lys Phe Pro Lys Ile Ala Val Lys Leu Lys Thr Leu Met Asp Val
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Gly Glu Ala Gln Arg Ile Lys Leu Ala Lys Glu Leu Ser Lys Lys Asp
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aca ggc aaa acc ctt tat att tta gat gag cct act acc ggt ttg cat
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Thr Gly Lys Thr Leu Tyr Ile Leu Asp Glu Pro Thr Thr Gly Leu His
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ttt gaa gac gtg aat cat ctt tta caa gtc ttg cat tct tta gtg gcg
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145	Lys				150			Lys		155					ΤÓΩ
Gly				165				Gln	170					T \2	
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Phe	Glu 210		Val	Asn	His	Leu 215	Leu	Glņ	Val	Leu	His 220	Ser	Leu	Val	Ala
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International Application No INTERNATIONAL SEARCH REPORT PCT/IB 00/00603 A. CLASSIFICATION OF SUBJECT MATTER
1PC 7 C12N15/10 C12Q1/68 C12N15/31 C12N1/19 C07K14/205 C07K16/12 A61K48/00 C12N15/86 G06F17/00 C12N1/21 A61K39/40 A61K39/106 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N C12Q C07K G06F A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, MEDLINE, CHEM ABS Data, BIOSIS, EMBL C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages 1-43 JAMES R. HUDSON ET AL.: "The complete set Υ of predicted genes from Saccharomyces cerevisiae in a readily usable form" GENOME RESEARCH, vol. 7, no. 12, December 1997 (1997-12), pages 1169-1173, XP002127444 the whole document

Further documents are listed in the continuation of box C.	X Patent family members are listed in annex.
Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report 1 1 10 00
27 September 2000	
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,	Authorized officer Montero Lopez, B

Fax: (+31-70) 340-3016

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	Relevant to claim No.
Category *	Citation of document, with indication, where appropriate, of the relevant passages	nesevant to Claim No.
Y	WO 97 37044 A (ASTRA AKTIEBOLAG) 9 October 1997 (1997-10-09)	1-3, 7-10, 14-20, 25,26, 30-38, 42,43
	page 2, line 11 - line 25 page 3, line 12 -page 16, line 15 page 16, line 21 -page 18, line 10 page 33, line 33 -page 34, line 14 page 64, line 22 - line 30	
Y	WO 98 26072 A (ELI LILLY AND COMPANY) 18 June 1998 (1998-06-18)	1,2,5, 7-9,12, 14-19, 22,25, 28, 30-37, 40,42,43
	page 2, line 1 - line 25 page 8, line 10 -page 9, line 2	·
Y .	EP 0 786 519 A (HUMAN GENOME SCIENCES, INC.) 30 July 1997 (1997-07-30)	1,2,4, 7-9,11, 14-19, 21,25, 27, 30-37, 39,42,43
	page 5, line 41 -page 7, line 7	
Y	BARTEL ET AL: "A PROTEIN LINKAGE MAP OF ESCHERICHIA COLI BACTERIOPHAGE T7" NATURE GENETICS,US,NEW YORK, NY, vol. 12, no. 12, January 1996 (1996-01), pages 72-77, XP002119798 ISSN: 1061-4036 the whole document	1,2,6-9, 13-19, 23-25, 28-37, 41-43
A .	MICHELINE FROMONT-RACINE ET AL.: "Toward a functional analysis of the yeast genome through exhaustive two-hybrid screens" NATURE GENETICS, vol. 16, July 1997 (1997-07), pages 277-282, XP002100296 the whole document	1-43
	-/	

INTERNATIONAL SEARCH REPORT

International Application No PCT/IB 00/00603

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Category *	Citation of document, with indication, where appropriate, or the relevant passages	
A	ROBERT M FREDERCKSON: "Macromolecular matchmaking: advances in two-hybrid and related technologies" CURRENT OPINION IN BIOTECHNOLOGY, vol. 9, no. 1, February 1998 (1998-02), pages 90-96, XP002127445 abstract page 90, left-hand column, paragraph 2 -right-hand column, paragraph 1 page 93, right-hand column, paragraph 2	1-43
	-page 94, right-hand column, paragraph 1	
.	WO 96 32503 A (THE GENERAL HOSPITAL CORPORATION) 17 October 1996 (1996-10-17) page 4, line 10 -page 7, line 23 page 18, line 28 -page 20, line 33 page 28, line 28 - line 34 page 29, line 14 -page 30, line 16 page 38, line 29 -page 39, line 25 page 43, line 34 -page 45, line 9 page 57, line 18 -page 62, line 4 page 78, line 19 -page 79, line 4	1-43
Α	JEAN-F. TOMB ET AL.: "The complete genome sequence of the gastric pathogen Helicobacter pylori" NATURE, vol. 388, 7 August 1997 (1997-08-07), pages 539-547, XP002062106 LONDON GB cited in the application	44-47, 55-58, 76,77, 79-87
X	table 2 -& DATABASE EMBL 'Online! Accession number 025047, 1 January 1998 (1998-01-01) XP002148640 the whole document	59-75, 83-87
	·	

INTERNATIONAL SEARCH REPORT

International application No. PCT/IB 00/00603

Sox I Observations where certain claims were found unsearchable (Continuation of item 1 of first sneet)
his International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1-43, 53, 54, 79, 80 and partially 44-47, 51, 55-57, 81-87 (inventions 1, 30, 32 and 33)
4. No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest.
Illumination and a same a same a same a same and a same a sam

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-43

Method for producing a collection of recombinant cell clones usable for two-hybrid systems using genomic DNA from a prokaryotic micro-organism; collection of cell clones so produced; use thereof in yeast two-hybrid systems, kit therefore and recombinant diploid yeast cell so obtained.

2. Claims: Partially 44-47, 51, 55-77, 81-87

Set of two polynucleotide and fragments thereof encoding polypeptide HP0047 of the left column of table I and polynucleotides and fragments thereof encoding interacting ORFs HP0047, HP0048 and HP0695 of the right column of table I; set of two corresponding polypeptides, protein-protein interaction and corresponding complex; computable readable medium having stored such interaction; use of such interacting polypeptides for identifying "selecting interacting domains SID" and SID of SEQ ID NO:68, 70, 72 of Table II and encoding polynucleotides of SEQ ID NO:67, 69, 71 of Table III and homologs thereof; uses thereof as primer or probe; vectors and host cells comprising the same; uses thereof for producing the polypeptides and polypeptides so obtained; uses of the polypeptides in screening assays for for identifying agents capable of modulating such protein-protein interaction; kit therefore and modulator agent so obtained; use of the polypeptides for the modulation of Helicobacter pylori's protein interaction; use for the production of antibodies and antibody so obtained; pharmaceutical compositions comprising any of the above mentioned polynucleotides, polypeptides, vectors, host cells, modulators and antibodies.

3. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0061 of the left column of table I and polypeptides HP0066, HP0978, and HP1409 of the right column of Table I; SID of SEQ ID NO:82, 84 and 86 of Table II and encoding polynucleotides of SEQ ID NO:81, 83 and 85 of Table III

4. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0064 of the left column of table I and polypeptide HP0063 of the right column of Table I; SID of SEQ ID NO:88 of Table II and encoding polynucleotide of SEQ ID NO:87 of Table III

5. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0066 of the left column of table I and polypeptide HP0066 of the right column of Table I; SID of SEQ ID NO:76 of Table II and encoding polynucleotide of SEQ ID NO:75 of Table III

6. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0067 of the left column of table I and polypeptides HP0069, HP0609, HP0768, HP0770 and HP0956 of the right column of Table I; SID of SEQ ID NO:196, 198, 200, 202 and 204 of Table II and encoding polynucleotides of SEQ ID NO:195, 197, 199, 201 and 203 of Table III

7. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0068 of the left column of table I and polypeptides HP0070 and HP0118 of the right column of Table I; SID of SEQ ID NO:64 and 66 of Table II and encoding polynucleotides of SEQ ID NO:63 and 65 of Table III

8. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0069 of the left column of table I and polypeptide HP0067 of the right column of Table I; SID of SEQ ID NO:74 of Table II and encoding polynucleotide of SEQ ID NO:73 of Table III

9. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0070 of the left column of table I and polypeptides HP0068 and HP0070 of the right column of Table I; SID of SEQ ID NO:262 and 264 of Table II and encoding polynucleotides of SEQ ID NO:261 and 263 of Table III

10. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0071 of the left column of table I and polypeptides HP0278, HP0417, HP0570, HP0775, HP1340 and HP1409 of the right column of Table I; SID of SEQ ID NO:142, 144, 146, 148, 150 and 152 of Table II and encoding polynucleotides of SEQ ID NO:141, 143, 145, 147, 149 and 151 of Table III

11. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0072 of the left column of table I and polypeptide HP1489 of the right column of Table I; SID of SEQ ID N0:256 of Table II and encoding polynucleotide of SEQ ID N0:255 of Table III

12. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0073 of the left column of table I and polypeptides HP0073, HP0232, HP0259, HP0067, HP0232 and HP0705 of the right column of Table I; SID of SEQ ID N0:154, 156, 158, 274, 276 and 278 of Table II and encoding polynucleotides of SEQ ID N0:153, 155, 157, 273, 275 and 277 of Table III

13. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0268 of the left column of table I and polypeptide HP1198 of the right column of Table I; SID of SEQ ID NO:78 of Table II and encoding polynucleotide of SEQ ID NO:77 of Table III

14. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0289 of the left column of table I and polypeptides HP0289, HP0887, HP0922, HP1038, HP1543, HP0610 and HP1355 of the right column of Table I; SID of SEQ ID N0:44, 46, 48, 50, 52, 54, 56, 58, 60 and 62 of Table II and encoding polynucleotides of SEQ ID N0:43, 45, 47, 49, 51, 53, 55, 57 and 61 of Table III

15. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0311 of the left column of table I and polypeptide HP0312 of the right column of Table I; SID of SEQ ID NO:194 of Table II and encoding polynucleotide of SEQ ID NO:193 of Table III

16. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0338 of the left column of table I and polypeptides HP0132 and HP0337 of the right column of Table I; SID of SEQ ID NO:166 and 168 of Table II and encoding polynucleotides of SEQ ID NO:165 and 167 of Table III

17. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0391 of the left column

of table I and polypeptides HP0392 and HP0392 of the right column of Table I; SID of SEQ ID NO:258 and 260 of Table II and encoding polynucleotides of SEQ ID NO:257 and 259 of Table III

18. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0691 of the left column of table I and polypeptides HP0692 and HP1362 of the right column of Table I; SID of SEQ ID NO:266 and 268 of Table II and encoding polynucleotides of SEQ ID NO:265 and 267 of Table III

19. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0697 of the left column of table I and polypeptides HP0012, HP0048, HP0558, HP0599, HP0696, HP0684, HP1037, HP1038, HP1299 and HP1576 of the right column of Table I; SID of SEQ ID NO:222, 224, 226, 228, 230, 232, 234, 236, 238 and 240 of Table II and encoding polynucleotides of SEQ ID NO:221, 223, 225, 227, 229, 231, 233, 235, 237 and 239 of Table III

20. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0776 of the left column of table I and polypeptides HP0067, HP0278, HP1378, and HP1409 of the right column of Table I; SID of SEQ ID NO:214, 216, 218 and 220 of Table II and encoding polynucleotides of SEQ ID NO:213, 215, 217 and 219 of Table III

21. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0797 of the left column of table I and polypeptides HP0289, HP0887, HP1349, HP1377 and HP1409 of the right column of Table I; SID of SEQ ID NO:184, 186, 188, 190 and 192 of Table II and encoding polynucleotides of SEQ ID NO:183, 185, 187, 189 and 191 of Table III

22. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0800 of the left column of table I and polypeptides HP0433, HP0687, HP0800, HP0801, HP0924, HP1267 and HP1460 of the right column of Table I; SID of SEQ ID NO:10, 12, 14, 16, 18, 20 and 22 of Table II and encoding polynucleotides of SEQ ID NO:9, 11, 13, 15, 17, 19 and 21 of Table III

23. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0801 of the left column of table I and polypeptides HP0152, HP0800 and HP1513 of the right column of Table I; SID of SEQ ID NO:24, 26, and 28 of Table II and encoding polynucleotides of SEQ ID NO:23, 25 and 27 of Table III

24. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0868 of the left column of table I and polypeptides HP0088, HP0327, HP0869, and HP1142 of the right column of Table I; SID of SEQ ID NO:2, 4, 6 and 8 of Table II and encoding polynucleotides of SEQ ID NO:1, 3, 5 and 7 of Table III

25. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0874 of the left column of table I and polypeptide HP0875 of the right column of Table I; SID of SEQ ID NO:254 of Table II and encoding polynucleotide of SEQ ID NO:253 of Table III

26. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0875 of the left column of table I and polypeptide HP0874 of the right column of Table I; SID of SEQ ID NO:212 of Table II and encoding polynucleotide of SEQ ID NO:211 of Table III

27. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0887 of the left column of table I and polypeptides HP0459, HP0610, HP0699, HP0887, HP1157, HP1460, and HP1464 of the right column of Table I; SID of SEQ ID NO:30, 32, 34, 36, 38, 40, 42, 242, 244, 246 and 248 of Table II and encoding polynucleotides of SEQ ID NO:29, 31, 33, 35, 37, 39, 40, 41, 241, 243, 245 and 247 of Table III

28. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0935 of the left column of table I and polypeptides HP0072, HP0528 and HP0657 of the right column of Table I; SID of SEQ ID NO:160, 162 and 164 of Table II and encoding polynucleotides of SEQ ID NO:159, 161 and 163 of Table III

29. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0978 of the left column of table I and polypeptides HP0979 and HP1583 of the right column of Table I; SID of SEQ ID NO:138 and 140 of Table II and encoding polynucleotides of SEQ ID NO:137 and 139 of Table III

30. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1032 of the left column of table I and polypeptides HP0643, HP0818, HP1122, HP1198 and HP1316 of the right column of Table I; SID of SEQ ID NO:122, 124, 126, 128 and 130 of Table II and encoding polynucleotides of SEQ ID NO:121, 123, 125, 127 and 129 of Table III

31. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1067 of the left column of table I and polypeptide HP0392 of the right column of Table I; SID of SEQ ID NO:210 of Table II and encoding polynucleotide of SEQ ID NO:209 of Table III

32. Claims: 53, 54, 79, 80 and partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1198 of the left column of table I and polypeptides HP0088, HP0268, HP0293, HP0452, HP0705, HP0775, HP0965, HP1032, HP1114, HP1124, HP1198, HP1274, HP1378, HP1411, HP1541 and HP1218 of the right column of Table I; SID of SEQ ID NO:90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 270 and 272 of Table II and encoding polynucleotides of SEQ ID NO:89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 269 and 271 of Table III

33. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1230 of the left column of table I and polypeptides HP1230 and HP1529 of the right column of Table I; SID of SEQ ID NO:132, 134 and 136 of Table II and encoding polynucleotides of SEQ ID NO:131, 133 and 135 of Table III

34. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1231 of the left column of table I and polypeptide HP1247 of the right column of Table I; SID of SEQ ID NO:120 of Table II and encoding

polynucleotide of SEQ ID NO:119 of Table III

35. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1244 of the left column of table I and polypeptides HP0857 and HP1246 of the right column of Table I; SID of SEQ ID NO:206 and 208 of Table II and encoding polynucleotides of SEQ ID NO:205 and 207 of Table III

36. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1246 of the left column of table I and polypeptides HP0121, HP0326, HP0407, HP0886, HP1035, HP1244 and HP1460 of the right column of Table I; SID of SEQ ID N0:170, 172, 174, 176, 178, 180 and 182 of Table II and encoding polynucleotides of SEQ ID N0:169, 171, 173, 175, 177, 179 and 181 of Table III

37. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1247 of the left column of table I and polypeptides HP1231 and HP1353 of the right column of Table I; SID of SEQ ID NO:250 and 252 of Table II and encoding polynucleotides of SEQ ID NO:249 and 251 of Table III

38. Claims: 52, 78 and partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1293 of the left column of table I and polypeptide HP1198 of the right column of Table I; SID of SEQ ID NO:80 of Table II and encoding polynucleotide of SEQ ID NO:79 of Table III

39. Claims: 48 and partially 44-46, 51, 55-57-59, 76, 77, 81, 82, 84-87

Set of two polynucleotides and fragments thereof encoding two Staphylococcus polypeptides; set of two corresponding polypeptides, protein-protein interaction and corresponding complex; computable readable medium having stored such interaction; use of such interacting polypeptides for identifying "selecting interacting domains SID" and polynucleotide encoding SID; uses of the polypeptides in screening assays for for identifying agents capable of modulating such protein-protein interaction; kit therefore and modulator agent so obtained; use of the polypeptides in the preparation of antibodies; antibodies so produced and pharmaceutical compositions comprising any of the above

mentioned polypeptides, polynucleotides, modulators or antibodies.

40. Claims: 49 and partially 44-46, 51, 55-57-59, 76, 77, 81, 82, 84-87

Idem as subject 39 for Streptococcus pneumoniae polypeptides and polynucleotides.

41. Claims: 50 and partially 44-46, 51, 55-57-59, 76, 77, 81, 82, 84-87

Idem as subject 39 for Escherichia coli polypeptides and polynucleotides.

42. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 interacting polypeptides not covered by the above mentioned subjects

INTERNATIONAL SEARCH REPORT

information on patent family members

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